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# California Medicine

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John W. Schulte, San Francisco.....	1968

**COUNCIL REPRESENTATIVES:**  
 Lewis T. Bullock, Los Angeles  
 Malcolm S. M. Watts, San Francisco  
**EX-OFFICIO:** Dwight L. Wilbur, San Francisco

## Executive Committee

Edward B. Shaw, San Francisco (Chmn.).....	1966
George C. Griffith, Los Angeles.....	1966
William W. Belford, San Diego.....	1967
Clayton G. Loosli, Los Angeles.....	1967
Victor Richards, San Francisco.....	1967
Justin J. Stein, Los Angeles.....	1967

**COUNCIL DESIGNEES:**  
 Lewis T. Bullock, Los Angeles  
 Malcolm S. M. Watts, San Francisco

## Committee on Nominations

Malcolm S. M. Watts, San Francisco (Chmn.).....	1966
Justin J. Stein, Los Angeles.....	1967
Stuart C. Knox, Los Angeles.....	1968

## Committee on Scientific Assemblies

William P. Longmire, Jr., Los Angeles.....	1966
George C. Griffith, Los Angeles.....	1966
John B. Dillon, Los Angeles.....	1967
Victor Richards, San Francisco (Chmn.).....	1967
David A. Rytand, Palo Alto.....	1967
John B. deC. M. Saunders, San Francisco.....	1968

## Committee on

### Continuing Medical Education

George C. Griffith, Los Angeles (Chmn.).....	1966
Alonzo J. Neufeld, Los Angeles.....	1966
Donald W. Petit, Los Angeles.....	1966
Victor Richards, San Francisco.....	1967
Saul J. Robinson, San Francisco.....	1968
John W. Schulte, San Francisco.....	1968

## Committee on CALIFORNIA MEDICINE

Grace B. Bell, Los Angeles.....	1966
Eugene M. Farber, Palo Alto.....	1966
Clayton G. Loosli, Los Angeles (Chmn.).....	1967
David Rubin, Los Angeles.....	1967
R. Kirklin Ashley, San Francisco.....	1967

## Committee on Scientific Information

Gerson R. Biskind, San Francisco.....	1966
L. S. Goerke, Los Angeles.....	1966
Justin J. Stein, Los Angeles (Chmn.).....	1967
Edmund L. Keeney, La Jolla.....	1968
Stuart C. Knox, Hollywood.....	1968

## Committee on Maternal and Child Care

Leland B. Blanchard, San Jose.....	1966
James W. Ravenscroft, San Diego.....	1966
Russell W. Mapes, Beverly Hills.....	1967
Keith P. Russell, Los Angeles (Chmn.).....	1967
Forrest H. Howard, Garden Grove.....	1967
Charles M. Blumenfeld, Sacramento.....	1968
Herbert A. Holden, San Leandro.....	1968

## Committee on Cancer

Burt L. Davis, Palo Alto.....	1966
Paul C. Samson, Oakland.....	1966
John W. Cline, San Francisco.....	1967
Robert W. Jamplis, Palo Alto.....	1967
David A. Wood, San Francisco (Chmn.).....	1967
John G. Walsh, Sacramento.....	1968

**SUBCOMMITTEE ON CANCER EDUCATION:** Sol R. Baker, Beverly Hills; Robert W. Jamplis, Palo Alto (Chmn.); Maurice Galante, San Francisco; Justin J. Stein, Los Angeles.

**SUBCOMMITTEE ON TUMOR TISSUE REGISTRY:** John W. Cline, San Francisco (Chmn.); Lewis W. Guiss, Los Angeles; James E. Kahler, Los Angeles; Carl M. McCandless, San Francisco; Weldon K. Bullock, Los Angeles.

**SUBCOMMITTEE ON CONSULTATIVE TUMOR BOARDS:** Bert L. Halter, San Francisco; Carl L. Moore, Bakersfield; Victor Richards, San Francisco; John G. Walsh, Sacramento (Chmn.).

## Committee on Dangerous Drugs and Adverse Drug Reactions

Charles H. Cutler, Sacramento.....	1966
Russell J. Tat, San Francisco.....	1966
Edward R. Bloomquist, Glendale.....	1967
Ralph O. Wallerstein, San Francisco.....	1967
John F. Murray, Fresno (Chmn.).....	1968

**SUBCOMMITTEE ON DANGEROUS DRUGS:** Edward R. Bloomquist, Glendale; Norman A. Gale, San Diego; Edward T. Jewett, Santa Rosa; William F. Quinn, Los Angeles (Chmn.); Helen B. Weyrauch, San Francisco.

**CONSULTANT:** Ralph Weilerstein, Berkeley

## BUREAU OF

## Research and Planning

Abe E. Berman, Sacramento  
 James C. Doyle, Beverly Hills  
 H. Russell Fisher, Glendale  
 Franklin F. Ham, Van Nuys  
 Paul I. Hoagland, Pasadena  
 James R. Powell, Stockton (Secty.)  
 John T. Saids, San Mateo  
 John J. Sheehy, Riverside  
 Samuel R. Sherman, San Francisco (Chmn.)

## EX-OFFICIO:

Ralph C. Teall, Sacramento  
 James C. MacLagan, San Diego  
 Carl E. Anderson, Santa Rosa  
**CONSULTANT:** Gerald W. Shaw, Santa Monica

## COMMISSION ON

## Professional Welfare

Bert L. Halter, San Francisco  
 George K. Herzog, Jr., San Francisco (Chmn.)  
 Edward Liston, Palo Alto  
 J. Norman O'Neill, Los Angeles  
 Dan Tucker, Oakland  
 Francis E. West, San Diego  
 James H. Yant, Sacramento (Secty.)

## Committee on Physicians Group Insurance

Homer C. Pheasant, Los Angeles.....	1966
Robert J. Westcott, El Centro.....	1967
Robert X. DeMangus, Glendale.....	1967
John B. Long, Sacramento.....	1967
George K. Herzog, Jr., San Francisco (Chmn.).....	1968
Arthur Kirchner, Los Angeles.....	1968

## Liaison Committee to Medical Schools

Bert L. Halter, San Francisco (Chmn.).....	1966
Alonzo Neufeld, Los Angeles.....	1966
Samuel R. Irvine, Beverly Hills.....	1967
Francis E. West, San Diego.....	1967
Frank J. Novak, Menlo Park.....	1968
Stanley Cowell, Los Angeles.....	1968

## EX-OFFICIO:

Ralph C. Teall, Sacramento  
 James C. MacLagan, San Diego  
 Carl E. Anderson, Santa Rosa

## Medical Review and Advisory Committee

Donald Donishorpe, Los Angeles.....	1966
Eugene M. Webb, San Francisco.....	1967
James H. Yant, Sacramento (Chmn.).....	1967
John Dillon, Los Angeles.....	1968
Carl Goetsch, Berkeley.....	1968

## Liaison Committee to State Bar of California

Robert J. McNeil, Los Angeles.....	1966
Henry A. Brown, San Mateo.....	1966
David Rubsam, Berkeley.....	1967
John V. Fiore, Westchester.....	1967
Francis E. West, San Diego (Chmn.).....	1968
Carl Goetsch, Berkeley.....	1968

## COMMISSION ON Allied Health Professions and Services

Charlotte C. Baer, San Francisco  
 Roger W. Barnes, Los Angeles  
 Forest J. Grunigen, Los Angeles (Chmn.)  
 Arthur A. Kirchner, Los Angeles  
 Thomas W. Ledwich, Napa  
 Wayne E. Pollock, Sacramento (Secty.)

## Committee on Paramedical Personnel

Gerson R. Biskind, San Francisco.....	1966
Carroll B. Andrews, Sonoma.....	1966
Arthur A. Kirchner, Los Angeles (Chmn.).....	1967
Frank C. Melone, Ontario.....	1967
Gregory Bard, San Francisco.....	1968
Elmer R. Jennings, Long Beach.....	1968
Charlotte C. Baer, San Francisco.....	1968

## Committee on Other Professions

Wayne E. Pollock, Sacramento (Chmn.).....	1966
John F. Murray, Fresno.....	1966
David Eder, Pasadena.....	1967
Burt L. Davis, Palo Alto.....	1967
C. Gerald Scarborough, San Jose.....	1968
William D. Evans, Los Angeles.....	1968

## Liaison Committee to California

### Medical Assistants Association

Richard H. Schug, Long Beach.....	1966
Judith D. Smith, Vallejo.....	1966
Sanford E. Feldman, San Francisco.....	1966
Leon O. Burke, Sacramento.....	1967
John C. Brennan, Pico Rivera.....	1967
H. Russell Irwin, San Diego.....	1967
Peary Benn Berger, Inglewood.....	1968
Charlotte C. Baer, San Francisco (Chmn.).....	1968

## Committee on Medicine and Religion

Ronald D. Smith, Fresno.....	1966
Frank J. Glassy, Sacramento.....	1966
Albert E. Long, Daly City.....	1967
Roger W. Barnes, Los Angeles (Chmn.).....	1967
Max Nelson, National City.....	1968

## Committee on Voluntary Health Agencies

Harold E. Wilkins, Downey.....	1966
J. Brandon Bassett, Oakland.....	1966
H. Mason Hohl, Beverly Hills.....	1967
Thomas W. Ledwich, Napa (Chmn.).....	1968

## Judicial COMMISSION

Douglas G. Campbell, San Francisco.....	1966
W. Philip Corr, Riverside (Secty.).....	1966
L. E. Wilson, Anaheim.....	1966
Donald A. Charnock, Los Angeles (Chmn.).....	1967
Albert E. Long, Daly City.....	1967
Donald Cass, Hollywood.....	1967
Floyd O. Due, Oakland.....	1968
Sidney J. Shipman, San Francisco.....	1968
Francis E. West, San Diego.....	1968

## COMMISSION ON Hospital Affairs

William L. Argo, Fresno  
 Lucius L. Button, Santa Rosa  
 James C. Doyle, Beverly Hills  
 Bert L. Halter, San Francisco (Chmn.)  
 John C. Lungren, Long Beach  
 Glenn Pope, Sacramento  
 Joseph W. Telford, San Diego

## Medical Staff Survey Committee

Robert M. Adams, San Leandro  
 William L. Argo, Fresno  
 Daniel W. Black, Castro Valley  
 Rush M. Blodgett, Jr., Redding  
 John A. E. Bullis, Los Angeles  
 Lucius L. Button, Santa Rosa  
 Bert L. Halter, San Francisco (Chmn.)  
 J. Ralph Hughes, San Diego  
 Wm. Kenneth Jennings, Santa Barbara  
 David B. Kuris, Los Angeles  
 Donald O. Lagerlof, Los Angeles  
 John C. Lungren, Long Beach  
 James W. Martin, Sacramento  
 William A. Newton, San Francisco  
 James L. Rhee, Oakland  
 John T. Saids, San Mateo  
 Wilfred J. Snodgrass, Santa Monica  
 Joseph W. Telford, San Diego

## Committee on Health Facilities Planning

James W. Dalton, Santa Barbara.....1966  
 Paul C. Doehring, Glendale.....1966  
 Pierre Salmon, San Mateo.....1966  
 Laurence A. Mosier, Garden Grove.....1967  
 John W. Gates, Visalia.....1967  
 Joseph W. Telford, San Diego.....1967  
 Jean F. Crum, Downey.....1968  
 Glenn A. Pope, Sacramento (Chmn.).....1968  
 Richard L. Taw, Los Angeles.....1968  
**CONSULTANTS:** Edward H. Crane, Jr., Inglewood;  
 John F. Murray, Fresno; Robert F. Schell, San Rafael.

## Finance Committee

Harold Kay, Oakland (Chmn.)  
 Roger C. Isenhour, San Diego  
 Frank C. Melone, Ontario  
 Joseph W. Telford, San Diego  
 Malcolm C. Todd, Long Beach

## Committee on Legislation

Dan O. Kilroy, Sacramento (Chmn.)  
 Stuart C. Knox, Los Angeles  
 Harold E. Wilkins, Downey  
 John Rumsey, San Diego  
 Samuel R. Sherman, San Francisco

## Advisory Board to Woman's Auxiliary

Ralph C. Teall, Sacramento (Chmn.)  
 James C. MacLagan, San Diego  
 Matthew N. Hosmer, San Francisco  
 William F. Quinn, Los Angeles  
 George A. Martin, Redding

## Benevolence Fund Operating Committee

Clyde L. Boice, Palo Alto (Chmn.)  
 Alexander Fraser, San Francisco  
 Elizabeth Mason Hohl, Los Angeles  
 Don C. Musser, San Francisco  
 George Wolf, Fresno  
 Dudley M. Cobb, Jr., Los Angeles



# Officers of Scientific Sections

Members who contemplate presentation of scientific papers should promptly address the secretary of the proper section at the address shown below.

## Allergy

John S. O'Toole.....Chairman  
3616 Main St., Riverside 92501  
Leo N. Meleyco.....Secretary  
2040 Forest Ave., San Jose 95128  
Ernest J. Saslow.....Assistant Secretary  
2011 - 18th St., Bakersfield 93301

## Anesthesiology

Bruce M. Anderson.....Chairman  
439 - 30th St., Oakland 94609  
Thomas W. McIntosh.....Secretary  
686 E. Union St., Pasadena 91101  
Donald B. Dose.....Assistant Secretary  
3585 - 4th Ave., San Diego 92103

## Dermatology

Paul M. Crossland.....Chairman  
1120 Montgomery Dr., Santa Rosa 95405  
Robert G. Walton.....Secretary  
1700 McHenry Village Way, Modesto 95350  
Samuel Ayres, III.....Assistant Secretary  
405 N. Bedford Dr., Beverly Hills 90210

## General Practice

Leland B. Blanchard.....Chairman  
678 E. Santa Clara, San Jose 95112

J. Blair Pace.....Secretary  
408 Cassidy St., Oceanside 92054  
Alfred F. Kandlbinder.....Assistant Secretary  
302 Via Paraiso St., Monterey 93940

## General Surgery

Newlin Hastings.....Chairman  
1138 W. 6th St., Los Angeles 90019  
Albert G. Clark.....Secretary  
450 Sutter St., San Francisco 94108  
David B. Sheldon.....Assistant Secretary  
1180 Fishe, Pacific Palisades 90272

## Industrial Medicine and Surgery

Rufus J. Walker.....Chairman  
740 S. Olive St., Los Angeles 90014  
Leon R. Rudnick.....Secretary  
15921 E. 14th St., San Leandro 94578  
Melvin R. Plancey.....Assistant Secretary  
555 S. Flower St., Los Angeles 90017

## Internal Medicine

Walter P. Martin.....Chairman  
211 Cherry Ave., Long Beach 90802  
Robert L. Paver.....Secretary  
384 Post St., San Francisco 94108  
John L. Benton, Jr.....Assistant Secretary  
1216 Wilshire Blvd., Los Angeles 90017

## Obstetrics and Gynecology

Karl L. Schaupp, Jr.....Chairman  
490 Post St., San Francisco 94102  
Lester T. Hibbard.....Secretary  
1930 Wilshire Blvd., Los Angeles 90057  
Warren E. Jones.....Assistant Secretary  
1380 - 45th St., Sacramento 95819

## Ophthalmology

Richard Kratz.....Chairman  
15225 Van Owen, Van Nuys 91405  
Victor G. Fellows.....Secretary  
595 Buckingham Way, San Francisco 94117  
Wendell C. Irvine.....Assistant Secretary  
3875 Wilshire Blvd., Los Angeles 90005

## Orthopedics

John F. Cowan.....Chairman  
2243 Van Ness Ave., San Francisco 94109  
David C. Monsen.....Secretary  
2300 S. Hope St., Los Angeles 90007  
Arthur R. Hartwig.....Assistant Secretary  
490 Post St., San Francisco 94102

## Otolaryngology

Thomas L. Soss.....Chairman  
333 N. San Mateo Dr., San Mateo 94401  
G. Howard Gottschalk.....Secretary  
8618 S. Sepulveda Blvd., Los Angeles 90045  
Charles P. Lebo.....Assistant Secretary  
490 Post St., San Francisco 94102

## Pathology

William C. Herrick.....Chairman  
233 A St., San Diego 92101  
Frank R. Dutra.....Secretary  
20103 Lake Chabot Rd., Castro Valley 94546  
William H. Kern.....Assistant Secretary  
679 S. Westlake Ave., Los Angeles 90057

## Pediatrics

Jack W. Bills.....Chairman  
14914 Sherman Way, Van Nuys 91405  
Richard L. Anderson.....Secretary  
636 Harris St., Eureka 95501  
Sherrad C. Swift.....Assistant Secretary  
14619 Whittier Blvd., Whittier 90605

## Physical Medicine

Gregory Bard.....Chairman  
UC Medical Center, San Francisco 94122  
Rene Cailliet.....Secretary  
4900 Sunset Blvd., Los Angeles 90027  
Herbert H. Cowper.....Assistant Secretary  
Dept. of Physical Medicine, U.C. Medical Center, San Francisco 94122

## Preventive Medicine

Byron O. Mork.....Chairman  
Room 6007, 1350 Front St., San Diego 92101  
Henrik L. Blum.....Secretary  
P.O. Box 871, Martinez 94554  
\*Herbert H. Cowper.....Assistant Secretary  
Los Angeles County Health Department  
220 N. Broadway, Los Angeles 90012

## Psychiatry and Neurology

George Y. Abe.....Chairman  
Metropolitan State Hospital, Norwalk 90650  
Werner M. Mendel.....Secretary  
1934 Hospital Pl., Los Angeles 90033

## Radiology

John C. Bennett.....Chairman  
2200 Hayes St., San Francisco 94117  
(St. Mary's Hospital)  
Victor G. Mikity.....Secretary  
1200 State St., Los Angeles 90033  
Vernon R. Gee.....Assistant Secretary  
2020 Court St., Redding 96001

## Urology

Carl Burkland.....Chairman  
5301 F St., Sacramento 95819  
Carl K. Pearlman.....Secretary  
1518 N. Sycamore, Santa Ana 92701  
James L. Goebel.....Assistant Secretary  
51 Loma Linda, Ross 94957  
\*Deceased

# Delegates and Alternates

TO THE AMERICAN MEDICAL ASSOCIATION

## DELEGATES

John G. Morrison, San Leandro.....(1965-1966)  
Arthur A. Kirchner, Los Angeles.....(1965-1966)  
Robert C. Combs, San Francisco.....(1965-1966)  
J. Norman O'Neill, Los Angeles.....(1965-1966)  
J. Lefe Ludwig, Los Angeles.....(1965-1966)  
Burt L. Davis, Palo Alto.....(1965-1966)  
Arlo A. Morrison, Ventura.....(1965-1966)  
James E. Feldmayer, Exeter.....(1965-1966)  
O. W. Wheeler, Riverside.....(1965-1966)  
Malcolm C. Todd, Long Beach.....(1965-1966)  
J. E. Vaughan, Bakersfield.....(1965-1966)  
Francis E. West, San Diego.....(1966-1967)  
Samuel R. Sherman, San Francisco.....(1966-1967)  
Henry Gibbons, III, San Francisco.....(1966-1967)  
John M. Rumsey, San Diego.....(1966-1967)  
Eugene F. Hoffman, Los Angeles.....(1966-1967)  
Warren L. Bostick, Los Angeles.....(1966-1967)  
J. B. Price, Santa Ana.....(1966-1967)  
Ralph C. Teall, Sacramento.....(1966-1967)  
James C. Doyle, Beverly Hills.....(1966-1967)  
Wilbur G. Rogers, Glendale.....(1966-1967)  
Charles B. Hudson, Oakland.....(1966-1967)

## ALTERNATES

Frederick Ackerman, Pleasant Hills.....  
Dudley M. Cobb, Los Angeles.....  
Emmett Rixford, San Francisco.....  
William F. Quinn, Los Angeles.....  
Harold Kay, Oakland.....  
Leon P. Fox, San Jose.....  
Henry Brown, San Jose.....  
Charles Grayson, Sacramento.....  
Wilbur Bailey, Los Angeles.....  
Alfred J. Murrieta, Jr., Los Angeles.....  
Joseph P. O'Connor, Pasadena.....  
Nicholas V. Oddo, Long Beach.....  
Albert G. Miller, San Mateo.....  
A. B. Sirbu, San Francisco.....  
Carl E. Anderson, Santa Rosa.....  
Joseph F. Boyle, Los Angeles.....  
Walter H. Brignoli, St. Helena.....  
Donald C. Dodds, Oakland.....  
Robb Smith, Orange Cove.....  
Homer C. Pheasant, Los Angeles.....  
Carl M. Hadley, San Bernardino.....  
Robert L. Watson, Jr., Los Angeles.....

(Delegates and Alternates to the AMA are elected for terms of two calendar years. Each office is scheduled for election at the Annual Session of the second year shown above.)

# Other Organizations and Medical Schools

## Board of Medical Examiners of the State of California

Secretary.....Shelby M. Hicks, M.D.  
1021 O Street, Room A202, Sacramento 95814  
San Francisco.....455 Golden Gate Ave.  
Room 4184 94102  
Los Angeles.....107 South Broadway 90012  
Sacramento.....1021 O Street, Room A547 95814

## The Public Health League of California

Executive Secretary.....Ben H. Read  
955 South Western Ave., Los Angeles 90006  
Associate Executive Secretary.....E. E. Salisbury  
693 Sutter Street, San Francisco 94102  
San Francisco.....693 Sutter Street 94102  
415 474-1061  
Los Angeles.....955 South Western Ave. 90006  
213 731-6397  
Sacramento.....1127 11th Street, 95814  
916 444-7496

## Department of Public Health of the State of California

Director.....Malcolm H. Merrill, M.D.  
2151 Berkeley Way, Berkeley 94704  
Berkeley.....2151 Berkeley Way 94704  
415 843-7900  
Sacramento.....631 J Street 95814  
916 442-4711  
Los Angeles.....703 State Building 90012  
213 620-2900

## Medical Schools in California

University of California School of Medicine, Medical Center, San Francisco 94122. Dean: William O. Reinhardt, M.D.  
Stanford University School of Medicine, 300 Pasteur Drive, Palo Alto 94304. Dean: Robert J. Glaser, M.D.  
University of Southern California School of Medicine, 2025 Zonal Avenue, Los Angeles 90033. Dean: Roger O. Egeberg, M.D.  
Loma Linda University School of Medicine, Loma Linda 92354. Dean: David Burd G. Hinshaw, M.D.  
University of California at Los Angeles, School of Medicine, Hilgard Avenue, Los Angeles 90024. Dean: Sherman M. Mellinkoff, M.D.  
California College of Medicine: 1721 Griffin Avenue, Los Angeles 90031. Dean: Warren L. Bostick, M.D.  
University of California, San Diego, School of Medicine, La Jolla 92038. Dean: Joseph Stokes, III, M.D.  
University of California at Davis, School of Medicine, Davis 95616. Dean: Charles John Tupper, M.D.

## California Medical Education and Research Foundation

Directors: Ralph C. Teall, M.D., President; Carl E. Anderson, M.D., Vice-President; Howard Hassard, Secretary; James C. MacLaggan, M.D.; Harold Kay, M.D.; William F. Quinn, M.D.; E. B. Shaw, M.D.



# Roster — CALIFORNIA COMPONENT MEDICAL SOCIETIES

Society secretaries are requested to notify California Medicine promptly when changes are indicated in their roster information

- ALAMEDA-CONTRA COSTA Medical Assn.,** 6230 Claremont Ave., Oakland 94618. Meets quarterly.  
J. Brandon Bassett.....President  
2930 McClure St., Oakland 94609  
Stanley R. Truman.....Secretary  
426 - 17th St., Oakland 94612
- BUTTE-GLENN Medical Society,** P. O. Box 1008, Chico 95927. Meets Fourth Thursday.  
Dale W. Ritter.....President  
6 Cohasset Circle, Chico 95926  
John Copeland.....Secretary  
1345 Longfellow Ave., Chico 95926
- FORTY FIRST Medical Society,** 9107 Wilshire Blvd., Beverly Hills 90210  
Paul D. Yates.....President  
844 Hermosa Ave., Hermosa Beach 90254  
Jordan M. Phillips.....Secretary  
11239 S. Lakewood Blvd., Downey 90241
- FRESNO County Medical Society,** 1118 Divisadero St., Fresno 93721. Meets Second Tuesday, 6:30 p.m., Sunnyside Country Club.  
Max Miller.....President  
3004 N. Fresno St., Fresno 93703  
Alan T. Sortor.....Secretary  
1340 E. Belmont St., Fresno, 93701
- HUMBOLDT-DEL NORTE County Medical Society.** Meets Second Thursday.  
Wells C. Carey.....President  
2822 E. St., Eureka 95501  
Max Todd.....Secretary  
616 14th St., Arcata 95521
- IMPERIAL County Medical Society.** Meets Second Tuesday, 8 p.m., Pioneer Memorial Hospital, Brawley.  
Robert S. Stone.....President  
426 Russell St., Brawley 92227  
Kenneth Glesne.....Secretary  
P.O. Box 1538, Heber 92249
- INYO-MONO County Medical Society.** Meets Fourth Tuesday except December, January, February.  
D. L. Christenson.....President  
380 N. Mt. Whitney Dr., Lone Pine 93545  
W. Ray Hartwig.....Secretary  
459 West Line, Bishop 93514
- KERN County Medical Society,** 2603 G Street, Bakersfield 93301. Meets Third Tuesday, 7:30 p.m., Society Office, 2603 G Street, except June, July, August.  
John R. Almklov.....President  
2441 G St., Bakersfield 93301  
M. Marlin Clark.....Secretary  
1402 Jefferson St., Delano 93215
- KINGS County Medical Society.** Meets Second Thursday, 7:00 p.m. Place to be announced.  
James Dean.....President  
912 N. Doury St., Hanford 93230  
W. S. Bridwell.....Secretary  
1028 N. Doury St., Hanford 93230
- LASSEN-PLUMAS-MODOC-SIERRA County Medical Society.** Meets on call.  
Kenneth G. Korver.....President  
50 N. Roop St., Susanville 96130  
James McCullough.....Secretary  
50 N. McDow St., Susanville 96130
- LOS ANGELES County Medical Assn.,** 1925 Wilshire Blvd., Los Angeles 90057.  
George C. Andersen.....President  
1925 Wilshire Blvd., Los Angeles 90057  
Jean F. Crum.....Secretary  
1925 Wilshire Blvd., Los Angeles 90057
- MARIN Medical Society,** 1601 Second St., Suite 106, San Rafael 94901. Meets First Thursday, 7:00 p.m.  
Robert Mills.....President  
711 D St., San Rafael 94901  
Robert F. Schell.....Secretary  
600 Mission Ave., San Rafael 94901
- MENDOCINO-LAKE County Medical Society.**  
Duane W. Bradley.....President  
Lakeshore Bldg, Lakeport 95453  
Patrick R. Allanson.....Secretary  
765 S. Dora St., Ukiah 95482
- MERCED County Medical Society.** Meets Fourth Thursday; meeting place changes.  
Earl B. Eager.....President  
2540 M St., Merced 95340  
Robert J. Schiffer.....Secretary  
656 W. 20th St., Merced 95340
- MONTEREY County Medical Society,** P. O. Box 308, Salinas 93903. Meets First Thursday.  
Joseph E. Turner.....President  
1010 Cass St., Monterey 93940  
Thomas S. Elliott.....Secretary  
101 Maple St., Greenfield 93927
- NAPA County Medical Society.** Meets Second Wednesday, P.O. Box 2158, Napa 94559.  
Richard G. Clark.....President  
3020 Beard Rd., Napa 94559  
Herbert Waechter.....Secretary  
980 Trancas St., Napa 94559
- ORANGE County Medical Association,** 300 S. Flower, Orange 92666. Meets First Tuesday, 7:00 p.m.  
Laurance A. Mosier.....President  
10510 Chapman Ave., Garden Grove 92640  
David I. Nielsen.....Secretary  
400 Westminster Ave., Newport Beach 92660
- PLACER-NEVADA County Medical Society.** Meets Second Wednesday.  
Bruce A. Becker.....President  
1166 High St., Auburn 95603  
Arthur R. Weaver.....Secretary  
701 High St., Auburn 95603
- RIVERSIDE County Medical Association,** 4175 Brockton Ave., Riverside 92501. Meets Second Monday, 7:30 p.m., Spanish Arts Gallery, Mission Inn.  
John C. Ivanoff.....President  
4024 12th St., Riverside 92501  
Richard W. Trotter.....Secretary  
6876 Magnolia Ave., Riverside 92506
- SACRAMENTO County Medical Society,** 5380 Elvas Ave., Sacramento 95819. Meets Third Tuesday, 8:30 p.m. Location of meetings varies.  
Orris S. Cook.....President  
1116 26th St., Sacramento 95816
- SAN BENITO County Medical Society.** Meets once a month, except July and August. Time and place to be announced.  
John J. Harris.....Acting President  
956 San Benito St., Hollister 95023  
Robert D. Quinn.....Secretary  
555 Monterey St., Hollister 95023
- SAN BERNARDINO County Medical Society,** 1875 N. D St., San Bernardino 92405. Meets First Tuesday, 7:30 p.m., Harold's Club, Fontana.  
Harold Hill.....President  
219 Cajon Ave., Redlands 92373  
Nicholas P. Krikes.....Secretary  
25060 Base Line, San Bernardino 92410
- SAN DIEGO County Medical Society,** 3427 - 4th Ave., San Diego 92103. Meets Second Tuesday. Location of meetings varies.  
Sam Peck.....President  
3427 4th Ave., San Diego 92103  
W. C. Herrick.....Secretary  
233 A St., San Diego 92101
- SAN FRANCISCO Medical Society,** 250 Masonic Ave., San Francisco 94118.  
George K. Herzog, Jr.....President  
2211 Post St., San Francisco 94115  
Nicholas D. Bonfilio.....Secretary  
1548 Stockton St., San Francisco 94133
- SAN JOAQUIN County Medical Society.** Meets First Thursday, 8:15 p.m., 445 W. Acacia St., P. O. Box 230, Stockton 95201.  
George Williams.....President  
400 S. Fairmont St. 95240  
Dora A. Lee.....Secretary  
2420 N. California St., Stockton 95204
- SAN LUIS OBISPO County Medical Society.** Meets Third Saturday, 7:00 p.m., Anderson Hotel, San Luis Obispo 95402.  
Harry J. Fryer.....President  
990 Pacific Ave., San Luis Obispo 93401  
Billy W. Mounts.....Secretary  
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- SANTA CLARA County Medical Society,** 700 Empey Way, San Jose 95128. Meets First Monday.  
Stanley A. Skillicorn.....President  
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550 Water St., Santa Cruz 95060  
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- SONOMA County Medical Society,** 1625 Franklin Ave., Santa Rosa 95404. Meets Second Thursday.  
Richard C. Barnett.....President  
450 Pitt St., Sebastopol 95472  
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1667 Bloomfield Rd., Sebastopol 95472
- STANISLAUS County Medical Society,** 303 Downey Ave., Modesto 95354. Meets Third Tuesday of the month, 7 p.m., Hotel Covell, Modesto.  
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108 Modesto Ave., Modesto 95354  
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References: 1. Ettenger, M. S.: Pennsylvania M.J. 66:35, 1963. 2. Data on file in the Medical Department of Warner-Chilcott Laboratories. 3. Jenkins, B. H.: J.A.M.A. 175:402, 1961. 4. Mann, P. H.: Current Therap. Res. 6:101, 1964. 5. Saltzman, M.: Clin. Med. 70:559, 1963. 6. Pullen, F. W. II: Eye Ear Nose & Throat Month. 42:38, 1963.



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## More Understanding in Genetics Reached in 1965

Scientists who try to understand life by studying its lowest common denominators made some important advances in 1965.

No one can yet answer the question: What is life? But this year, for the first time, scientists put together a synthetically-produced model of a nucleic acid—one of the lowest common denominators—and saw it reproduce in the test tube.

The first synthesis of a self-reproducing component of living matter was achieved at the University of Illinois Center for Advanced Study.

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Sol Spiegelman, Ph.D., and coworkers assembled a self-propagating, infectious ribonucleic acid of the bacterial virus Q-beta. Ribonucleic acid (RNA) is one of the complex chemicals on which the heredity of living organisms is coded; the other is deoxyribonucleic acid (DNA). Virus Q-beta, one of the group of viruses called bacteriophage because they attack bacteria, is an organism whose genetic coding is carried on RNA.

(In most living organisms the basic genetic code is DNA-borne and RNA acts as a messenger between the DNA master plan and the cell machinery. As far as is known, RNA carries the master plan only in some viruses. The nucleic acid in a virus is surrounded by a protein coat. When a virus attacks a bacterial cell it leaves the protein coat outside after "injecting" the nucleic acid. The viral nucleic acid takes over the genetic machinery of the cell and uses it to direct the cell to produce more viral nucleic acid and viral protein coats. Eventually, the cell disrupts, spilling the assembled viruses into the extra-cellular environment where they can attack more cells.)

Dr. Spiegelman and his group said the key to synthesis was a purified enzyme, a chemical taking part in chemical reactions but not changing itself.

The enzyme, RNA-dependent-RNA-polymerase ("replicase" for brevity) was induced in the bacteria *Escherichia coli* by infecting the cells with virus Q-beta. Replicase is a natural product of virus Q-beta infection; it is the "runner" which helps to assemble copies of viral nucleic acid according to viral RNA instructions in the invaded cell. Purified enzyme was then mixed with RNA from Q-beta virus and component chemicals of which RNA is made. No bacterial cells were present in the mixture and no virus.

With the viral RNA acting as template or pattern, the enzyme assembled component chemicals into new strands of RNA. Subsequent experiments proved that the synthesized RNA was as competent as viral RNA in acting as a template for the formation of still more synthesized nucleic acid.

To complete the proof that the synthesized RNA was identical to the original viral RNA, experiments were conducted which showed that virus particles produced by the synthetic RNA were of the same serological type as authentic Q-beta.

Explaining the significance of the work, aside from the fact that synthesis of nucleic acid was actually achieved, Dr. Spiegelman said:

"For the first time a system has been made available which permits the unambiguous analysis of the molecular basis underlying the replication of a self-propagating nucleic acid. Until now we searched indirectly. It was like fumbling inside a black box. Now we can know what to do."

Dr. Spiegelman predicted that methods soon will be developed to permit the synthesis of self-replicating DNA.



**utions and adverse reactions:** The transitory drowsiness which occur with hydroxyzine HCl usually disappears spontaneously a few days with continued therapy, or is correctable by dosage reduction. Dryness of the mouth may be seen with higher doses. Transitory motor activity, including rare instances of tremor and convulsions, has been reported, usually on higher than recommended dosage. Hydroxyzine HCl may potentiate barbiturates, narcotics such as meperidine, and other CNS depressants. In canine use, dosage for these drugs should be decreased. Because drowsiness may occur, patients should be cautioned against driving or operating dangerous machinery. **Parenteral Solution**  
**utions and contraindications:** This dosage form is intended for intramuscular (I.M.) or intravenous (I.V.) administration and should not under any circumstances be injected subcutaneously or intra-arterially. When usual precautions for I.M. injection have been followed, reports of soft tissue reactions have been rare. Due to infrequent reports of, and, rarely, reversible hemolysis with hemoglobinuria, arising from too rapid intravenous administration of the solution, administration should be slow, no faster than 25 mg. per minute and should not exceed 100 mg. in any single dose. Particular care should be used to insure injection only into intact veins; a number of digital gangrene occurring distal to the injection have been attributed to inadvertent intra-arterial injection or arterial extravasation, both of which should be avoided.

## "Smart Pills" Are On the Way

Improved and more effective tranquilizers that do not produce drowsiness or other undesirable side effects will some day be available. Indeed, these future drugs affecting the nervous system and our moods will be aimed toward specific clinical indications. Some will be designed to aid in concentration, improve the memory, and accelerate the thinking process. These so-called "smart pills" will also increase alertness during stressful periods and also assist slow learners and retarded persons. Others will remove grief and sadness, and some may be useful in alcoholism and other character disorders. Austin Smith, M.D., in *Emory University Quarterly* (21:136-137), Summer 1965.

## Color Slide Available On Eye Safety

You are taking an unnecessary risk to your eyesight if your eyeglasses fail to provide protection against accidental injuries to your eyes. A soft rubber ball, tossed by a child, can shatter a lens of ordinary eyeglasses and the fragments might penetrate the eyes.

This advice comes from the Division of Accident Prevention, Public Health Service, Department of Health, Education, and Welfare. The Division says the danger can largely be averted by wearing glasses with heat-treated glass lenses or plastic lenses, fitted in sturdy, non-flammable frames. The cost is not much more than ordinary eyeglasses.

The advantages of safety glasses for reading, street wear, or protection against the sun are discussed in a new color slide series called "RX For Eye Safety." This visual unit has been developed by the Division of Accident Prevention of the Public Health Service, and the National Society for the Prevention of Blindness.

"Anyone with a visual disorder should take extra precautions against the possibility of further impairment of his eyesight," says Dr. Paul V. Joliet, Chief, Division of Accident Prevention, Public Health Service. "Far too few of the millions of Americans who wear eyeglasses or sunglasses have the kind which provide protection against accidental injury as well as correction for their eyesight. The sooner all eyeglasses are of the safety variety the better."

The new slide series is intended to be shown before school groups of at least junior high school level, service and social organizations, and religious groups, among others.

Sets may be obtained through the National Society for the Prevention of Blindness, 16 East 40th Street, New York, New York 10016, or your local or State Health Department office.



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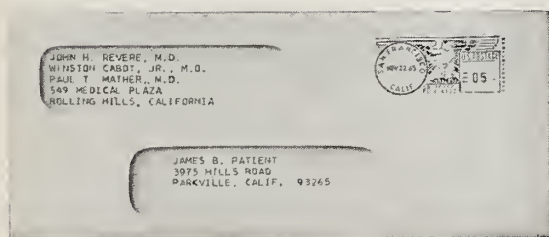
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## Herpes Simplex—Problem for Wrestlers

Efforts are being made to control the spread of herpes simplex, a skin infection which hit hard last winter among high school and college wrestling teams in the northeastern U.S.

Wrestlers seem to have a special susceptibility to the infection because of close bodily contact.

Herpes simplex usually isn't dangerous. It is recognized as the common cold sore. But for wrestlers, the infection is more than a nuisance. The skin lesions can spread rapidly from wrestler to wrestler. Sometimes painful, they may be accompanied by fever, chills, and general malaise.

Wrestling meets were widely disrupted last winter when the infection was at its peak. The only remedies are strict hygiene and removal of the infected athlete from participation.

The November 29 *Journal of the American Medical Association* contains articles by physicians at the Universities of Maryland and North Carolina and Dartmouth College, describing outbreaks among wrestlers.

A statement outlining herpes symptoms and preventive measures has been issued to team physicians and coaches by the American Medical Association's Committee on the Medical Aspects of Sports.

The Committee's recommendations, based essentially on the information documented in these JAMA articles, have already been sent to collegiate wrestling coaches and team physicians with the encouragement that a special program of prevention be instituted for the 1965-66 season.

In addition, the National Federation of State High School Athletic Associations forwarded the recommendations to its constituents to check a possible outbreak at the high school level.

The president of the AMA, James Z. Appel, M.D., was particularly interested in the problem. He is team physician of Franklin and Marshall College in his hometown of Lancaster, Pa.

W. Roy Phillips, the Franklin and Marshall wrestling coach, pointed out that several meets had been cancelled and others postponed in the Eastern Intercollegiate Wrestling Association, of which the college is a member.

Partly in response to a request by the E.I.W.A., a statement on herpes simplex was developed by the AMA committee.

The statement urges coaches and athletes to be alert for signs of herpes infection. It asks physicians to restrict athletes' participation when there is a hazard of infection. It also notes, however, that athletic participation should be encouraged if, in the physician's judgment, the danger of infection is only "remotely serious."

Herpes simplex diagnosis is sometimes difficult, the statement points out, because it may be con-

(Continued on Page 32)

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**Contraindications:** Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

**Precautions:** *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

**Side effects:** Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

*Benactyzine hydrochloride*—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

*Meprobamate*—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

**Dosage:** Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

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Before prescribing, consult package circular.

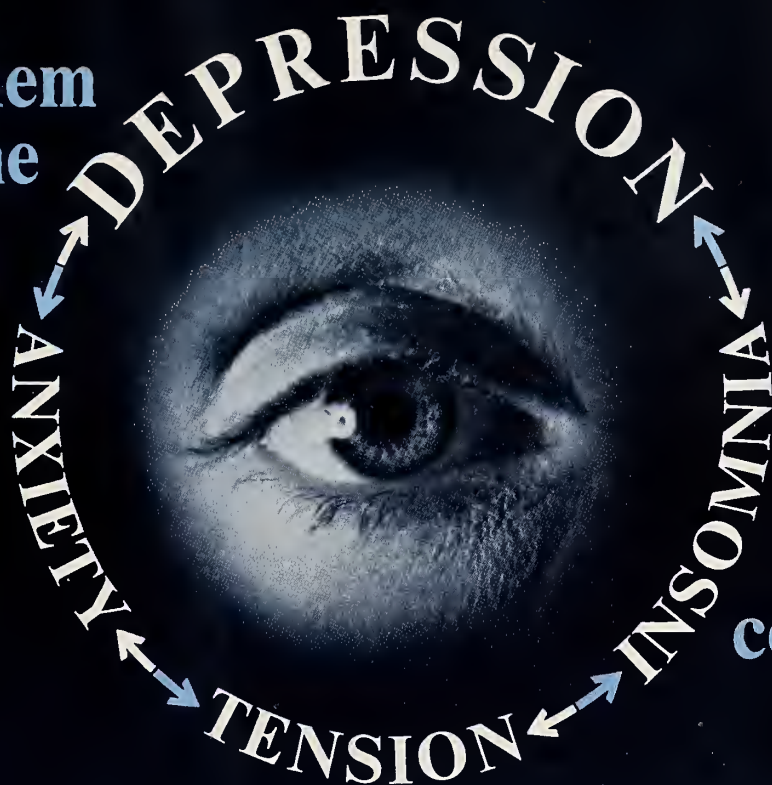


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Monrovia, California

### Clinical Investigation Government Style

A new drug may not be shipped across state borders for administration to a human until the sponsor of the drug (who may be the investigator) has filed a request for exemption for such use with the FDA. . . . He must describe and identify the source of the drug and its manufacturer; he must describe previous animal studies with the drug to show that it is reasonably safe to initiate human studies; he must give evidence of his professional qualifications and his facilities for investigation. Finally, the investigator must certify that he will obtain consent from the persons receiving the drug except where this is not feasible or, in the investigator's best judgment, is contrary to the best interests of the subjects. The sponsor must also make progress reports at appropriate intervals, not exceeding a period of one year. He must promptly report any adverse effect which is reasonably regarded as due to the drug. He must maintain records for a period of two years after the drug has been approved or disapproved, or after his investigations have been discontinued. Joseph F. Sadusk, Jr., M.D. to Association of Military Surgeons, November 17, 1965.

### Herpes Simplex—Problem for Wrestlers

(Continued from Page 30)

fused with other skin or systemic diseases or may be obscured by other infections.

Usually the "cold sores" are merely unpleasant cosmetically, somewhat painful, and disappear in about 10 days unless superinfected by staphylococci or other organisms. With wrestlers, two to three weeks may pass before the skin is clear.

Why are wrestlers particularly vulnerable to herpes simplex? Perhaps because of the sweaty contact and frequent skin abrasions of the sport, the statement said. A more virulent strain of the herpes simplex virus may have been encountered, it added.

Studies show that sores invariably appear first at sites of frequent wrestling contact, such as the side of the face and on the forearms. According to available evidence, wrestling mats and wearing apparel aren't transmitters of infection. The virus is passed directly from person to person.

The statement recommends that:

1. Coaches and wrestlers be especially alert for herpes simplex infection during the coming season.
2. Physicians be ready to arrive at prompt provisional diagnoses. The presence of tell-tale cells can be determined quickly by microscopic examination.
3. Infected wrestlers should be removed from participation until their skin clears.
4. Reporting and recording of suspected and confirmed cases should be improved.
5. A fundamental hygiene program for all wrestlers should be emphasized.



## ACROMEGALY

### The Effects of Various Steroid Hormones on the Insulin-Induced Growth Hormone Response

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GEROLD M. GRODSKY, PH.D., AND PETER H. FORSHAM, M.D., *San Francisco*

■ *The availability of a sensitive assay for human growth hormone has made it possible to directly measure the effects of various agents purported to alter growth patterns. Acromegalic patients present a special problem both in early diagnosis and in therapy. Being able to measure growth hormone in these patients provides an accurate index of activity and a precise measure of therapeutic effectiveness.*

*In an attempt to determine whether a pituitary block of growth hormone secretion is feasible in this condition, a study was made of the effects of estrogen, androgen and glucocorticoid administration on growth hormone response to a standard insulin tolerance test in a patient with active acromegaly. In the dosage schedules used in this study, it was not possible to suppress either basal growth hormone secretion or blunt its responsiveness to the normal physiologic stimulus of hypoglycemia.*

THERE ARE CONFLICTING reports in the literature regarding the effects of various steroid hormones on growth, and, more recently, on circulating levels of growth hormone. With the advent of a sensitive radioimmunoassay for growth hormone<sup>6</sup>

and the development of a standard physiologic "stress test" for growth hormone secretion,<sup>8</sup> it is now possible to define such effects more precisely. The lack of studies documenting the effects of steroid hormones on growth hormone secretion in acromegaly, and the frequently disappointing results of conventional treatment for this condition, prompted us to make this report.

The effects of estrogen, androgen and glucocorticoid administration on the insulin-induced

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growth hormone response in a patient with active acromegaly were determined 12 months after unsuccessful pituitary irradiation. The patient selected for study was ideal in that his growth hormone responsiveness to the physiologic stimulus of insulin-induced hypoglycemia was preserved, a phenomenon found in some but not all persons with acromegaly.<sup>9</sup>

## Report of a Case

A 27-year-old soldier on active duty first noted change in his physical features in 1958, at age 20. These changes consisted of enlargement of the tongue, hands, feet and neck, and coarsening of the facial features. During the ensuing two years, his glove size increased from 5 to 7, shoe size from 7½ to 9, neck circumference from 15½ to 17, and hat size from 6½ to 7. He also noted a deepening of his voice accompanied by voice fatigue, the development of an underbite and a decrease in libido. Sweating was a constant problem and fatigability a major complaint.

In spite of these symptoms, the patient did not seek medical attention, and his condition stabilized by 1960. It was not until 1963, when he consulted a physician for an injured finger, that acromegaly was diagnosed. At that time excessive sweating, impaired libido and frequent dull headaches were his major complaints.

Physical examination revealed the classic features of acromegaly. Blood pressure was 140/60 mm of mercury and the pulse regular at 82 per minute. No visceromegaly or papillomas of the skin were evident. No abnormalities were noted on fundoscopic and neurological examinations.

Routine laboratory data, including hemograms, urinalysis, x-ray films of the chest and an electrocardiogram were within normal limits, as were the blood urea nitrogen, fasting blood sugar and result of a glucose tolerance test. Except for the serum phosphorus, which ranged between 5.2 and 5.6 mg per 100 ml, the serum electrolytes were normal. X-ray films of the skull showed enlargement of the frontal sinuses and sella turcica with thinning of the posterior clinoid processes. The heel pad was 22 mm thick. Protein-bound iodine was 6.2 mcg per 100 ml. Radioactive iodine uptake at 24 hours was 27 per cent. Twenty-four hour urinary gonadotropin was greater than 50 millimicrons but less than 100 millimicrons. Urinary excretion of 17-hydroxycorticoid was within normal limits at 11 mg per 24 hours but the 17-keto-

steroid value was elevated at 43 mg, later at 39 mg, per 24 hours. Urinary excretion of calcium and phosphorus was normal. A fasting serum growth hormone value was 62 millimicrograms per ml.

During the patient's first stay in hospital, in the fall of 1963, a right ureteral calculus developed and passed spontaneously. An intravenous pyelogram showed a dilated right ureter which subsequently reverted to normal.

Conventional 200 KV x-ray therapy with 3,040 roentgens to the pituitary fossa was undertaken from 12 August to 20 September 1963. In 18 months of observation after completion of radiation therapy, there was no detectable regression of the patient's acromegalic features and no lessening of the symptoms of excessive sweating and fatigability. Serum phosphorus values remained above 5.0 mg per 100 ml and the normal diurnal phosphate variation was absent. Fasting growth hormone values did not return to normal.

## Materials and Methods

The effects of short- and long-term administration of estrogen, androgen and dexamethasone on growth hormone levels, both fasting and insulin-stimulated, were studied.

A fasting insulin tolerance test, using 0.1 unit of regular insulin per kilogram of body weight, given by intravenous infusion, was used as the standard stimulus for growth hormone secretion. This dose was found to be adequate for the patient in the present case, as he had no evident insulin resistance. Specimens were obtained for glucose and growth hormone analysis at 15 to 30 minute intervals for 2 hours during each test period.

Glucose was determined by a glucose oxidase method and growth hormone was assayed by the radioimmunologic technique described by Hunter and Greenwood,<sup>4,6</sup> and modified by Grodsky<sup>5</sup> to employ growth hormone-I<sup>125</sup> and the separation of bound and free hormone by preferential precipitation with Na<sub>2</sub>SO<sub>4</sub>.

The study continued for six months. The protocol was designed to measure the effects of various treatment schedules with estrogen, androgen and a glucocorticoid on growth hormone responsiveness. Two to four weeks intervened between the steps in the test procedure. The patient remained active, followed a standard diet and main-



tained a stable weight during the entire period of study.

After the baseline insulin tolerance test, the effect of an acute intravenous dose of estrogen was determined. Premarin,<sup>®</sup>\* 40 mg, was given intravenously 30 minutes before the insulin was administered. The effect of long-term estrogen administration on the morning growth hormone levels was then determined by giving increasing doses of an estrogen by mouth for one month and measuring the fasting growth hormone at weekly intervals. The estrogen used was Premarin,<sup>®</sup> 1.25 mg at first, then increasing by the same amount weekly to a total of 5.0 mg.

The effect of androgen pretreatment was determined by insulin tolerance testing performed three weeks after an intramuscular injection of 600 mg of testosterone propionate.

A three-week course of dexamethasone, 1.0 mg every eight hours, was used to test the effect of glucocorticoid administration on the standard test procedure.

The dosages of these hormones were chosen as those which would be feasible for long-term treatment if a significant block in growth hormone secretion could be achieved.

## Results

A fasting serum growth hormone value, obtained one year before the present study and before pituitary radiation therapy, was available for comparison with values at the time of study. The original growth hormone level was 62 millimicrograms per ml, 10 times the maximum normal level.

The results of the control test are listed in Table 1. Maximum hypoglycemia occurred within the first 30 minutes, and the growth hormone peak rose 40 millimicrograms per ml above the baseline value.

An identical test performed two days later was preceded by an intravenous infusion of 40 mg of Premarin<sup>®</sup> 30 minutes before the insulin was given. The results of this test are shown in Table 2. The hypoglycemic response was not as great as in the control test, but in spite of this there was a brisk growth hormone response of 32 millimicrograms per ml above the baseline value at 45 minutes.

To determine the effect of long-term oral estrogen therapy on serum growth hormone, weekly in-

creases of Premarin<sup>®</sup> from 1.25 mg to a final daily dose of 5.0 mg were preceded by fasting growth hormone determinations. The four-week series showed the fasting blood sugar to be fairly constant, ranging from 82 to 88 mg per 100 ml. The corresponding growth hormone levels were likewise quite constant, ranging from 35 to 38 millimicrograms per ml. During the fourth week of

TABLE 1.—*Baseline Insulin Tolerance Test (0.1 Units per kg of Body Weight)*

Time (minutes)	Glucose (mg/100 ml)	Growth Hormone (m $\mu$ g*/ml)
0	78	65
30	32	95
45	32	90
60	54	85
90	73	105
120	78	62

\*Millimicrograms.

TABLE 2.—*Insulin Tolerance Test After Intravenous Infusion of 40 mg of Premarin<sup>®</sup>*

Time (minutes)	Glucose (mg/100 ml)	Growth Hormone (m $\mu$ g*/ml)
—30 (Premarin <sup>®</sup> infusion)		
0	88	48
30	50	75
45	64	80
60	72	65
90	88	59
120	84	....

\*Millimicrograms.

TABLE 3.—*Insulin Tolerance Test 21 Days After a Single Intramuscular Injection of 600 mg Testosterone Propionate*

Time (minutes)	Glucose (mg/100 ml)	Growth Hormone (m $\mu$ g*/ml)
0	103	36
30	36	25
45	59	27
60	85	87
90	92	....
120	102	45

\*Millimicrograms.

TABLE 4.—*Insulin Tolerance Test After Giving 1.0 mg Dexamethasone Every 8 Hours for 21 Days*

Time (minutes)	Glucose (mg/100 ml)	Growth Hormone (m $\mu$ g*/ml)
0	93	55
15	57	56
30	21	113
45	....	....
60	84	213
90	115	73
120	99	128

\*Millimicrograms.

\*Conjugated equine estrogens, Ayerst Laboratories, New York City, N. Y.

estrogen administration, gynecomastia developed; it subsided promptly on discontinuance of the hormone.

A large dose of testosterone propionate (600 mg) was administered intramuscularly 21 days before the third insulin tolerance test. The results are shown in Table 3. A sharp hypoglycemic response occurred at 30 minutes, followed by the highest growth hormone peak at 60 minutes, 51 millimicrograms per ml above the baseline value.

Glucocorticoid effect was determined by pretreatment with 1.0 mg dexamethasone given orally every 8 hours for 21 days before repeating the insulin tolerance test. The results of this test, as shown in Table 4, again reveal failure of the pretreatment to blunt the growth hormone response. In fact, the maximal growth hormone response at 60 minutes was the highest value of the test series, 158 millimicrograms per ml above the baseline value. However, the decrease in blood sugar was least with this test. It is also noteworthy that the baseline fasting growth hormone levels remained significantly elevated after each of the pretreatment schedules.

## Discussion

It has been shown in normal subjects that the serum growth hormone level rises during hypoglycemia.<sup>8</sup> Moreover, growth hormone secretion can be increased similarly by a hypoglycemic stimulus in some, but apparently not all acromegalic patients.<sup>9</sup> This observation has been confirmed by observations in a series of acromegalic patients in whom growth hormone was measured by the radioimmunoassay technique used in the present case.<sup>5</sup> As insulin resistance may occur in acromegaly, an augmented insulin tolerance test is frequently necessary to induce hypoglycemia. Fortunately in the present case both normal insulin sensitivity and the physiologic responsiveness to hypoglycemia were preserved. Thus, by utilizing a standard insulin tolerance test, the effects of pretreatment with various hormones on somatotropin secretion could be assessed.

The hormones chosen for this study are known to have specific pituitary blocking properties, but the possibility that they might also have an inhibitory effect on growth hormone has not been thoroughly explored. Such a phenomenon of "hormonal overlap" in pituitary feedback has previously been considered.<sup>3,12</sup> If such a pituitary block of

growth hormone secretion could be demonstrated, it might have a practical therapeutic application.

Estrogen administration has been considered in the past to be effective in controlling impaired carbohydrate tolerance and other clinical and metabolic effects of acromegaly.<sup>7</sup> Studies of sulfation factor activity in acromegaly have also been reported as being favorably influenced by estrogen administration.<sup>1</sup> Such reports seem to suggest a block in growth hormone production and are thus in accord with the clinical impression of those who have administered estrogens in an attempt to prevent excessive height at the time of the adolescent growth spurt.<sup>13</sup> This apparent effect of estrogens has not been pursued with studies using a sensitive growth hormone assay.

In contrast, androgen therapy has been used to promote height in children with growth retardation.<sup>11</sup> There have been, however, studies to show that a more rapid advancement of bone than height age is apt to occur with androgen administration.<sup>10</sup> We recently observed a pronounced rise of growth hormone in response to hypoglycemia in a patient with prepubertal growth retardation treated with testosterone.<sup>2</sup>

It has long been recognized that high therapeutic doses of glucocorticoids are associated with delayed growth in children. More recently it has been shown that cortisol administration actually can suppress growth hormone secretion,<sup>12</sup> but whether such an effect can be achieved in an acromegalic patient and whether it may be of practical therapeutic value has not yet been assessed.

The studies reported herein disclose that in a patient with active acromegaly, in whom the growth hormone response to the physiologic stimulus of hypoglycemia is preserved, a variety of agents may be tested for their effectiveness in blocking this response. It is of interest that growth hormone secreting tumors, unlike most other endocrine tumors, may maintain responsiveness to a normal physiologic stimulus. The magnitude of response to insulin-induced hypoglycemia could not be blunted by administration of either estrogen or androgen in the form and dosage we used. Administration of a glucocorticoid in a dose equivalent to more than 60 mg per day of cortisol has been shown to be effective in inhibiting the release of growth hormone in normal subjects.<sup>12</sup> Dexamethasone in an amount equivalent to 80 mg of cortisol per day, administered for three weeks, did not block the growth hormone response to the



standard insulin tolerance test. Therefore a glucocorticoid dose greater than that shown to be effective in suppressing growth hormone in normal individuals was without effect in the acromegalic subject.

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# Hemorrhage During Long-Term Anticoagulant Drug Therapy

## Part 1. Intracranial Hemorrhage

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■ *Intracranial hemorrhage was the most serious hemorrhage as measured by death and disability, occurring during long-term anticoagulant drug therapy of 1,626 patients. Among 95 hemorrhagic episodes considered life-threatening or potentially crippling, 30 were intracranial and 56 were gastrointestinal. Over two-thirds of the patients with intracranial hemorrhage died, as against one-tenth of those with gastrointestinal hemorrhage.*

*The incidence of intracranial hemorrhage is increased among hypertensive patients, but the results of a controlled study indicate that the incidence of intracranial hemorrhage is not affected by whether or not the hypertensive patient is receiving anticoagulant therapy. Hypertension is the important precipitating factor, not the prothrombin level. Even at excessively low prothrombin levels only one intracranial hemorrhage occurred in 337 instances.*

*In this series, reducing coagulability to a desirable range did not increase the probability of intracranial hemorrhage. Once bleeding occurred, however, it increased the risk of death and disability.*

VIGOROUS APPRAISAL of the benefits of long-term coumarin therapy has limited the indications for such treatment to only a few conditions. The same intense appraisal has not been applied to the dangers based on the risk of hemorrhage, the chief hazard of coumarin therapy. The frequency of bleeding is often emphasized, but without precise data as to the actual incidence, without distinction between serious and minor hemorrhage and without em-

phasis on the need for a vascular break before bleeding may occur. It is far more important to identify or to suspect potential or actual bleeding lesions before anticoagulant drug therapy is started than to investigate thoroughly after bleeding has occurred.

This study will consider only the risks of hemorrhage after long-term therapy. Gangrenous necrosis of the skin, a rare hemorrhagic complication, has occurred only in the first few days after starting treatment, not as a delayed complication of prolonged therapy. Similarly hemopericardium is

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This article on Hemorrhage During Long-Term Anticoagulant Drug Therapy is in five parts. Part II is scheduled to appear in the February issue.



TABLE 1.—*Distribution and Mortality Rate of Serious Hemorrhages (Life-Threatening or Potentially Crippling) During Long-Term Anticoagulant Drug Therapy*

	Patients	Intracranial Hemorrhages			Gastro-intestinal Hemorrhages			Other Hemorrhagic Deaths	Other Serious Non-fatal Hemorrhages	Serious Hemorrhages (Total)	
		No.	Per Cent	Died	No.	Per Cent	Died			No.	Per Cent
Various diseases .....	366	7	1.9	4	11	3.0	0	1 Intra-abdominal	1 Retro-peritoneal	20	5.4
Coronary arterial disease .....	973	15	1.5	12	29	2.9	2	1 "Leaking aneurysm"	1 Hemothorax 1 "Subendocardial" 1 Pancreas 1 Kidney	49	5.0
Cerebral vascular disease .....	287	8	2.8	5	16	5.6	3	1 Adrenal 1 Retro-peritoneal		26	9.0
Total .....	1626	30		21	56		5	4	5 <sup>†</sup>	95	5.8

usually confined to the treatment of acute myocardial infarction, and is rarely seen during long-term therapy. Minor hemorrhage—such as surface bleeding, capillary oozing or slight hematuria—has not proved to be a precursor of dangerous "spontaneous" hemorrhage. This will be discussed in a subsequent study in this series. The risk of the primary disease, if untreated or if treatment is discontinued, is usually serious disability or death. The comparable risk from anti-coagulant therapy is life-threatening or potentially crippling bleeding—true "serious" hemorrhage. It is important to develop a realistic estimate of the incidence of serious hemorrhage after anticoagulant therapy, and to determine how successfully this risk can be avoided. Serious *but avoidable* hemorrhage cannot be cited as valid contraindication to anticoagulant drug therapy.

### Incidence of Serious Hemorrhage

Ninety per cent of serious hemorrhages (those that are potentially crippling or fatal) are either intracranial or gastrointestinal (Table 1).<sup>\*</sup> Intracranial hemorrhage, although less frequent, is more often fatal and is therefore the subject of the first study in this series.

The incidence of such hemorrhage and any correlation with hypertension or with the level of hypocoagulability will be considered. Subsequent studies will be concerned with gastrointestinal hemorrhage, with the significance of minor bleeding, with the selection and management of patients and with unusual clinical experiences with this therapy.

<sup>\*</sup>Reference Nos. 2, 4, 6, 7, 9, 12, 16, 17, 21-23.

### Material

In a series of 1,626 patients collected from other studies who received long-term anticoagulant drug therapy, there were 95 serious hemorrhages, of which 30 were intracranial (Table 2). Although it is widely believed that nearly all intracranial hemorrhages occurring during anticoagulant therapy result in death, nine of the 30 survived. Oddly, this is a better survival rate than found among patients with spontaneous intracranial hemorrhage in a recent study in Connecticut. Of 68 patients with intracranial hemorrhage in that report, only 12 (18 per cent) survived one month.<sup>5</sup> These groups obviously are not comparable as treated and control groups, but the results are still seemingly paradoxical, since the effect of anticoagulants on intracranial hemorrhage should be to increase mortality.

*What Are the Clinical Correlates of Intracranial Hemorrhage?*—Intracranial hemorrhage is a natural complication of hypertension and would be expected to occur more frequently among hypertensive patients on long-term anticoagulant drug

TABLE 2.—*Site and Mortality Rate in 30 Cases of Intracranial Hemorrhages Occurring During Long-Term Anticoagulant Drug Therapy*

	No.	Died	Lived
Cerebral or intracerebral hemorrhage .....	22	19	3
Possible intracranial bleeding .....	1	...	1
Intracranial bleeding .....	1	1	...
Possible intracerebral hemorrhage .....	1	...	1
Subarachnoid hemorrhage .....	4	1	3
Subdural hemorrhage .....	1	...	1 <sup>*</sup>
	30	21	9

<sup>\*</sup>Operation done.

TABLE 3.—Data from Four Reported Series of Intracranial Hemorrhage in Hypertensives in Treated and Control Groups on Long-Term Anticoagulant Drug Therapy

Author	Number of Treated	Number of Controls	Number of Hypertensives		Number of Intracranial Hemorrhages			
			Treated	Controls	Treated		Controls	
					No.	Died	No.	Died
Bjerkelund <sup>2</sup> .....	119	118	32	28	3	3	3	1
Millikan <sup>10</sup> .....	115	115	"... essentially identical for ... degrees and extent of hypertension ..."		....	6	....	7
Suzman, <sup>21</sup> Ruskin and Goldberg .....	779	1111	Not definitely stated		5	Not stated*	10	Not stated*
Hill, Marshall, and Shaw <sup>8</sup> .....	71	71	24	24	5	5†	0	....
Fisher <sup>6</sup> .....	196	184	114	115	5	....	3	....
Total .....	1280	1599			24		23	

\* Millikan reported only the fatal hemorrhages.

† Two were originally unrecognized cerebral hemorrhages.

therapy. Available controlled studies comparing the incidence of intracranial hemorrhage among hypertensive patients receiving long-term anticoagulant drug therapy and among untreated hypertensive patients (Table 3) show no significant difference in incidence of intracranial hemorrhage for the two groups. These findings indicate the importance of controlled clinical studies, for without such studies the 24 intracranial hemorrhages occurring in the treated group could have been attributed to the anticoagulant drug therapy.

Since even control studies may be open to the criticism of bias, statistically these reports can only be suggestive. The levels of prothrombin activity were not correlated with the hemorrhages. Although Millikan<sup>10</sup> did not give the levels of prothrombin activity, he said that "perhaps what these figures actually say, or reflect, is the fact that these patients [with cerebral hemorrhages] were hypertensive and did have diseased intracranial vessels." This idea is also expressed by other investigators.<sup>12,21,22</sup>

Fisher<sup>6</sup> in an analysis of all types of hemorrhage, mild and serious, concluded that "provided that the prothrombin level is maintained above 15 per cent (Quick one-stage test) anticoagulation is no more dangerous in hypertensive patients than in normotensives." He did not specifically relate prothrombin activity to intracranial hemorrhage.

The critical level of hypocoagulability below which serious hemorrhage is likely to occur has not been precisely determined. Owren<sup>13,14,15,16</sup> expressed belief it is 10 per cent by the prothrombin-proconvertin method. (This is equivalent to 20 per cent by the Quick one-stage method or a pro-

thrombin time in seconds of twice the control figure minus 2.<sup>18</sup> Owren<sup>13,14,15,16</sup> found in an analysis of more than 1,000 cases with prothrombin-preconvertin (P-P) levels below 10 per cent that all four coagulation factors reduced by the coumarin drug (Factors II, prothrombin; VII, proconvertin; IX, plasma thromboplastin component; X, Stuart-Prower Factor) were below their individual "safe levels."

If hemorrhages can be initiated by deficiency of any of these four factors below their supposed "safe" levels, serious hemorrhage would be expected to be frequent in patients with hypocoagulability below 10 per cent by the P-P test or 20 per cent by the Quick one-stage test.

*What Is the Relation of an "Unsafe" Level of Prothrombin Activity to the Onset of Intracranial Hemorrhage?*—Unfortunately, the correlation of hemorrhage with the prothrombin level is usually based on tests made after the hemorrhage, a finding invalid for several reasons: First, the prothrombin level may have been in the safe range before hemorrhage; afterward it may be low because of loss of thrombotic elements.<sup>3,19,20</sup> Second, a single low reading obtained after hemorrhage does not indicate how often the same reduction may have occurred previously without the patient having serious bleeding. Third, and most important, a cerebral vascular lesion may be present which could bleed even at normal levels of coagulability.

Bjerkelund<sup>3</sup> expressed belief that the risk of thrombosis is better indicated by the number of tests at which the prothrombin activity exceeds the clinical level than by a single test following throm-



TABLE 4.—Data from Four Reported Series on Frequency of Spontaneous Intracranial Hemorrhage Anticoagulant Drug Treatment in Relation to Times the Prothrombin Activity was Below the (20 Per Cent Quick One-Stage or 10 Per Cent P & P Test)

Authors	Diagnosis	Patients	Total Number of Tests	At "Safe" Levels	Results of Prothrombin Tests*			
					Below "Safe" Levels		Intracranial Hemorrhage (All Patients Died)	
					No.	Per Cent	At "Safe" Levels	Below "Safe" Levels
Bjerkelund <sup>2</sup> .....	Myocardial Infarction	119	11649	10654	995	8.5	3	2
Borchgrevink <sup>4</sup> .....	Angina Pectoris	103	2428	2115	313	12.9	0	0
Moseley, et al. <sup>11</sup> .....	Various	300	2668	2454	214	8.0	1	0
Askey <sup>1</sup> .....	Various	100	4326	3863	463	10.6	0	0
Total .....		622	21071	19086	1985	9.4	4	2

\* Average interval between tests: Bjerkelund, 1 to 3 weeks; others, 4 weeks.

bolic complication. Similarly, the risk of hemorrhage is better gauged by the frequency of its occurrence at periods of excessive prothrombin reduction rather than from single readings obtained after hemorrhage.

Accordingly, the frequency of spontaneous intracranial hemorrhage has been estimated in 622 patients in whom a total of 21,071 prothrombin tests were made (Table 4) at intervals of three weeks to a month.<sup>1,2,4,11</sup> The percentages of low readings in the four series here combined were 8.5, 12.9, 8 and 10.6 and the average was 9.4 per cent. These patients, therefore, were exposed to excessively low levels of prothrombin activity during nearly one-tenth of these tests. In the 1,985 periods of excessive reduction of prothrombin, there were only two episodes of intracranial hemorrhage.

*What Is the Relation of an "Unsafe" Level of Prothrombin Activity to the Onset of Intracranial Hemorrhage in Hypertensive Patients?—*In one

of these series (119 cases) Bjerkelund<sup>2</sup> separated his findings on hypertensive and normotensive patients; I did the same on the last 100 patients so treated in private practice (Table 5). Among the 45 patients in these two groups with diastolic blood pressure over 100 mm of mercury, there were 337 instances of prothrombin reduction below 10 per cent (prothrombin-proconvertin test) or below 20 per cent (Quick one-stage method) with only one intracranial hemorrhage at this low level. (Two others occurred at a "safe" level.) Among the 174 normotensive patients in the two groups, there were 1,121 instances of excessive reduction with one such hemorrhage. In the 10,981 instances of a "safe" level of prothrombin activity, there was one intracranial hemorrhage.

In the absence of controlled series, these figures merely reflect what one would expect—that the lower the hypocoagulability, the greater the number of overt intracranial hemorrhages. This is true whether the patients be normotensive or hyper-

TABLE 5.—Frequency of Spontaneous Intracranial Hemorrhage in Hypertensives and Normotensives in Relation to Prothrombin Test Results

	Prothrombin Tests					
			Number At "Safe" Level	Number Below "Safe" Level	Intracranial Hemorrhage (All Patients Died) At "Safe" Level	Below "Safe" Level
	Patients	Total Number				
HYPERTENSIVES*						
Bjerkelund <sup>2</sup> .....	32	3204	2929	274	2	1
Askey <sup>1</sup> .....	13	669	606	63	0	0
Totals .....	45	3873	3535	337	2	1
NORMOTENSIVES						
Bjerkelund <sup>2</sup> .....	87	8445	7724	721	1†	1‡
Askey <sup>1</sup> .....	87	3657	3257	400	0	0
Totals .....	174	12102	10981	1121	1	1

\* Diastolic blood pressure over 100 mm of mercury.

† Bleeding caused by glioblastoma shown at autopsy.

‡ Diabetes and generalized arteriosclerosis (PP test—3 to 4 per cent)

lled clinical studies of hypertensive  
" and "low" levels of hypocoagu-  
y obva are not feasible.

## Discussion

Intracranial hemorrhage, although infrequent, is the most dangerous of the life-threatening or potentially crippling complications of long-term anticoagulant drug therapy. Yet, the risk of intracranial hemorrhage among patients receiving anticoagulant drug therapy is comparable to the risk in untreated patients; the risk is increased predominantly among the hypertensives in each group.

Among 219 patients separated according to blood pressure, three intracranial hemorrhages occurred among the 45 hypertensives and two among the 174 normotensives (Table 5).

The risk in normotensive patients is apparently negligible unless there is an unrecognized underlying cerebral lesion. In over 10,000 instances when the prothrombin activity was at a desirable level in normotensives, only one intracranial hemorrhage occurred. (The bleeding was into a glioblastoma.) In over 1,000 instances when the prothrombin level was excessively low, only one intracranial hemorrhage occurred (Table 5).

Although the risk in hypertensive patients is higher, controlled clinical studies show no significant increase of such cerebrovascular accidents in treated patients compared with untreated patients (Table 3). The risk was low in this hypertensive group regardless of the level of prothrombin activity. There were only two intracranial hemorrhages during 3,535 "safe" test periods. There was only one instance of intracranial hemorrhage during 337 periods when the prothrombin level was excessively reduced (Table 5).

This evidence indicates that anticoagulant therapy does not increase the frequency of intracranial hemorrhage in hypertensives but does increase the seriousness. The risk of an intracranial hemorrhage occurring is apparently the risk associated with hypertension; if hemorrhage occurs, the intensity of the bleeding increases and nearly all patients die.

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# Office Treatment of Lower Extremity Injuries

## *A View of Feasibility, Limitations and Hazards*

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■ *The injuries to the lower extremities seen in a surgical office may be classified as contusions, lacerations, sprains, lesions of tendons and their sheaths, involvement of bursae, chronic muscle fatigue, infections and deformities of the nails, leg ulcers, and fractures of the ankle, foot and toes.*

*The treatment of these conditions in an office will vary under different circumstances, but one should be guided by certain fundamental rules. Contusions are best treated by the application of elastic compression bandages. Extensive lacerations should be explored under local anesthesia with the tourniquet in place, injured tissue excised, and the wound sutured. Ankle sprains should be strapped. Immediate hospitalization must be considered in all moderate to severe initial sprains to the knee. Lesions of bursae usually respond to the injection of hydrocortisone preparations. The same treatment is used in chronic muscle fatigue, plus immobilization of the part. Chronic recurrent infection and deformities of the nails are treated by removal of the nail under local anesthesia. Fractures of the ankle, the foot and toes may be reduced under local anesthesia and a cast applied. If further swelling is feared, the patient should be put in hospital immediately.*

THE EXTENT AND LIMITATION of care that can be given in the office to patients with injuries of the lower extremities depends largely on the personnel and equipment available there. The necessary increasing costs of hospital emergency room services, which for the most part can be provided at greater convenience to both patient and physician in well-equipped surgical offices, should en-

courage physicians to eliminate expensive personal office units and join with other physicians to form a more economical and more efficient facility that several of them may use in common.

Since they differ in many ways from those applicable to treatment in hospital, the general rules for treatment of lower extremity injuries in a well equipped office will be reviewed.

First, the surgeon must make an earnest effort to find out exactly how the injury was caused, even though the patient is reluctant or seems unable to

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give a good account. This should be made a separate paragraph in the patient's history, entitled "Mechanism of Injury." It then becomes an important diagnostic and legal record.

Every examination of the lower extremities must include an evaluation of the arterial pulses and the status of the venous return.

## Burns

Patients with burns of any extent or severity should be admitted to hospital immediately. Minor burns are covered with Vaseline gauze, and then compression bandages are applied.

## Contusions

Contusions are treated most satisfactorily by meticulously applied compression bandages. After protection of the contused area with sterile dressings, half-thickness cotton wool is applied to cover the entire extremity. This may be done by making it into roller bandages or applying it as sheets. In contusions below the knee, the compression dressing should be applied from the metatarsal heads to the knee. In contusions of the thigh of any magnitude, this dressing should be extended from the toes to the groin. Woven elastic bandages are then applied in a spiral fashion, taking care that they are applied with firmness but not so tight as to constrict. Compression bandages of this type stay in place, seldom requiring adjustment by the patient. Should adjustment become necessary, the inner dressing and the cotton wool protective dressing do not need to be removed. Webril,<sup>®</sup> sheet wadding and similar commercially prepared rolls applied beneath a compression bandage do not give the uniform compression nor do they have the elasticity of cotton wool, and often ridges occur beneath the spiral turns. In cases where additional local compression is desired, a pattern may be cut from sheets of sponge rubber and applied over the cotton wool.

Properly applied, dressing of the kind here described eliminates most of the hazard of arterial compression, a condition especially to be guarded against in the elderly and in patients with circulatory deficiencies.

Before being sent home, the patient is instructed to keep the extremity elevated most of the time.

*Limitations.* Contusions with large hematomas of the buttocks, groin and popliteal space are best treated in hospital, with the use of closed suction.

Even so, absorption of the mass may be slow. For hematomas of the groin and popliteal space, repeated aspiration may be necessary.

The prescription of alternate cold and hot applications leaves too much to the motivation, intelligence and facilities of many ambulatory patients.

## Puncture and Penetrating Wounds, Foreign Bodies, Lacerations

Recent puncture and penetrating wounds should be gently explored for the presence of foreign bodies. Frequently, puncture wounds of the plantar surfaces of the feet contain bits of the shoe or sock. Removal of these particles at the first visit may prevent infection and suppuration.

Whether deep-lying metallic foreign bodies should be removed is a matter of surgical judgment. If removal is decided against, the reasons should be clearly explained to the patient and assurances made that the foreign body can be removed later if it causes troublesome symptoms.

Removal of a deep-lying metallic foreign body, no matter what its apparent position, never should be considered a simple surgical task. It is always best to determine the probable position with several x-ray views taken after needles have been inserted in three planes to provide orienting points. The surgical procedure is always performed under tourniquet technique.

Most lacerations may be sutured under infiltration or block anesthesia. Large lacerations must be explored and debrided, with hemostasis established under tourniquet technique. Lacerations occurring in the region of joints should be splinted for eight to ten days, preferably by a cast.

*Hazards.* The use of prophylactic antibiotics should be considered for earth workers and those in slaughter houses and fisheries. A tetanus toxoid booster is given in all cases in which the time lapse since the last booster is too long or the way in which the wound was caused is in question. For patients who have not had tetanus immunization and have a wound about which there is question of tetanus infection should be given human tetanus antitoxin.

## Hip and Knee Sprains, Tendinitis, Bursitis

Sprains of the hip joint are rare. This diagnosis should not be made before thorough x-ray studies



of the hip joint are carried out and it is ascertained that the lower back is not the source of the symptoms.

Sprains of the adductor muscles, either unilateral or bilateral, are not infrequent. These are an entity and the occurrence of pain on motion of the hip should not confuse the diagnosis. Localized tenderness is present in the region of the origin of the muscles and pain occurs when the muscle is called into action against resistance. The differential diagnosis should exclude femoral hernia and venous thrombosis.

The varieties of injuries following indirect or direct violent trauma to the knee joint do not permit of simple classification. Sprains of the ligaments about the knee joint are frequently accompanied by synovitis. Often in cases of moderate to severe injury it is not possible to make a definite and accurate diagnosis at the first examination. A reasonable diagnosis is "synovitis—acute, traumatic." Initial acute injuries to the knee joint, followed by rapidly appearing intra-articular fluid, are best handled in the office only as an emergency. If the joint is tense, aspiration should be done, compression bandages applied and weight-bearing on the injured extremity forbidden. The patient should be put in hospital immediately and placed in Buck's traction with a compression bandage in place. Further aspiration may be necessary.

In recurring synovitis of the knee joint, a more conservative course may be followed until a definite diagnosis is established. However, following the injury, weight-bearing should be forbidden, compression bandages applied and aspiration performed as necessary. It should be remembered in the later treatment of these patients that properly applied lifts to the shoes may be an essential part of the treatment.

Tendinitis and bursitis in the popliteal space are manifested by localized tenderness and pain when the involved structures are required to act against resistance. Persistent pain in the popliteal area without localizing signs may present an exceedingly baffling problem. The various symptoms may make one suspect a Baker's cyst, but the presence of such a lesion may be very difficult to prove. If the possibilities of popliteal aneurysm and arterio-venous fistula have been excluded and aspiration of the popliteal space permits withdrawal of synovial fluid, then a definite diagnosis of Baker's cyst may be made.

A definite diagnosis to explain the underlying disease in a persistently painful knee may be exceedingly difficult to establish. This may be true even when cysts or tears of the cartilage are present. Complete x-ray studies should be carried out as soon as flexion of the knee permits. Arthrotomy should not be performed until a reasonably certain diagnosis has been established. The use of a properly applied cylinder cast permits more comfortable ambulation and gives further time for the establishment of a definite diagnosis—or for the symptoms to abate. It should be remembered that as long ago as 1909, Sir Robert Jones preached that although a cartilage may not heal, a patient may.

To be expected in cases of this kind are prolonged treatment and some permanent disability in patients in the upper age brackets, prolonged disability in arthritic knees, and permanent quadriceps atrophy.

### The Ankle and Forefoot

Sprains of the ankle are caused by inversion and they involve one or more components of the lateral ligaments. They vary greatly in severity. Severe sprains are best treated by efficiently applied strapping, which must run at least to the upper third of the leg. The patient should be supplied with crutches and told to keep the extremity elevated most of the time. Elastic compression bandages and anklets are poor substitutes for strapping. For very severe sprains, a short leg cast should be applied.

One should be suspicious in the case of any inversion sprain where there is tenderness on the medial surface of the ankle joint. Excessive soft tissue swelling should cause one to discard the diagnosis of sprain, at least temporarily. In any case, where the nature and extent of the lesion is in doubt, thorough x-ray studies should be done and stress films should be made even if the procedure requires a short general anesthetic.

As to sprains of the forefoot, unless they are definitely mild, x-ray studies of the foot should be made, for severe sprains are frequently accompanied by tarsal or metatarsal fractures.

*Myositis and Tendinitis.* Classic myositis crepitans is seen in the extensors of the ankle, foot and toes, most frequently in workers who constantly press pedals in the operation of machines. The condition is caused by repeated mild internal trauma

which produce an acute stage of muscle fatigue. Basically, the pathologic change is edema, plus fibrin deposition plus increased lactic acid formation. The grating, or crepitation, is caused by the tearing of the fibrin threads when the muscle contracts. The milder of these conditions respond to the injection of local anesthesia and hydrocortisone into the affected areas. Rest of the part is essential. In moderate to severe cases, the injection of local anesthesia and hydrocortisone must be accompanied by total immobilization of the part, preferably in a plaster cast, and this must include immobilization of the toes. The cast is left in place 10 to 14 days. Further injections, if thought necessary, may be made through a window in the cast.

*Affections of the Soleus Group.* Stress injuries in the soleus muscles are frequently (often erroneously) diagnosed as ruptures of the plantaris muscle. Also to be guarded against is attributing the symptoms to venous thrombosis. These injuries may occur when seemingly minor stress is involved, as in running backward. The symptoms are dramatically sudden in onset and usually immediately disabling. The patient often believes that a thrown object has hit him in the calf. The site of pain and tenderness varies from the lower border of the popliteal space to the region of the distal musculo-tendinous junction, usually more pronounced medially. Often ecchymosis appears in 12 to 48 hours. The treatment for the milder cases is compression bandaging, the use of crutches and an adequate raise on the heel of the shoe. For more severe cases a short leg cast should be applied with the foot in the equinus position. Prolonged immobilization in this position, however, is to be avoided. At the end of three weeks the cast should be bi-valved and active motion of the ankle permitted.

*Paratenitis of the Achilles Tendon.* This may follow repetitive movement or direct violence to the structure. Injection of local anesthesia and hydrocortisone into the affected area and partial or complete immobilization in the equinus position is usually effective. In the more severe cases and in recurrent cases, light x-ray therapy in divided doses has given relief.

To be guarded against is missing the diagnosis of a rupture of the Achilles tendon. If the tendon is intact, compression of the calf muscle between

the fingers causes spontaneous plantar flexion of the foot.

*Bursitis, Tenosynovitis.* Trochanteric bursitis and tendinitis are definite lesions. At times the symptoms are vague and the diagnosis is somewhat difficult to establish. The patient should be examined while lying on the side as well as while standing. The treatment is injection with local anesthesia and hydrocortisone and rest, as indicated.

Tenosynovitis of the tendons about the ankle joint is treated in the same manner. Here, however, in the moderate to more severe cases, cast immobilization for 10 to 14 days may be necessary. Chronic recurrence may necessitate surgical intervention.

*Painful Heel, Calcaneal Spurs, Bursitis, Plantar Fasciitis.* Injection with a mixture of local anesthetic and hydrocortisone is effective for these conditions, provided other static deformities of the foot are corrected and proper footwear is worn. A satisfactory method of relieving pressure from the plantar surface of the os calcis is to have an efficient shoemaker remove the heel and excavate the sole of the shoe and the heel over an area sufficiently large to protect the trigger point area beneath the os calcis. Use of heel inserts and pads is usually not as satisfactory.

## Injuries to the Nails

*Paronychia.* It is not necessary to incise the sulci or to remove a wedge from the side of the nail in suppurative paronychia. Usually, adequate drainage is established by gently teasing the eponychium away from the nail with the back end of a pointed scalpel. Usually this can be done without anesthesia if it is started in an area away from the inflammatory site and carried out slowly and gently.

Subungual hematoma should be drained by drilling with a burr or burning a hole at the base of the nail with a heated end of a paper clip.

Subungual hematomas are not infrequently the result of fractures of the terminal phalanx, and a fracture connecting with a hematoma is a compound fracture. Therefore, precise sterile precautions should be taken when opening subungual hematomata.

Chronic recurring paronychia and deformities of nails following injury which do not respond to



conservative treatment, are best treated by removal of the entire nail.

## Fractures

Simple fractures about the ankle joint may be reduced under local anesthesia and a cast applied. Undisplaced fractures of the metatarsals are treated with a walking cast.

Fractures of the phalanges are treated by strapping the adjacent toes together with adequate padding between them. A metatarsal bar may be applied to the sole of the shoe and the patient allowed to ambulate with cane or crutches.

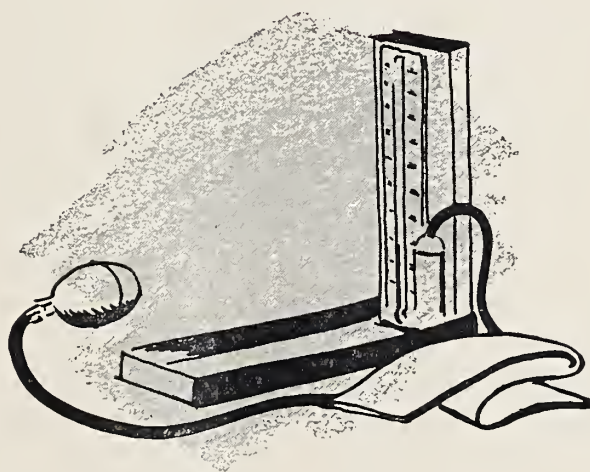
One of the hazards in such cases is increasing swelling after the application of the cast. When there is any fear of this, or the patient's level of intelligence or his home conditions are such that proper elevation cannot be assured, a day or two in hospital, for elevation of the extremity and observation, is advisable.

## Chronic Leg Ulcers

In dealing with chronic leg ulcers, the lesion should be covered with Vaseline gauze and a compression bandage applied. Elevation should be insisted upon, the patient to be put in hospital if necessary to make sure that this instruction is carried out. As soon as the base of the ulcer is clean, a split thickness graft is applied. In most cases the graft is not sutured but is held in place with properly applied pressure dressings. The leg must be kept elevated and a compression bandage continued. If stasis is present or is to be feared after the ulcer has healed, a zinc gelatin (Unna®) case should be applied and renewed every two to three weeks until the skin covering has thickened sufficiently.

**AUTHOR'S NOTE:** Because of the scope of the subject, some general statements have been made. Their fallibility is recognized.

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# Prevention of Mental Disorder

## The Role of the General Practitioner

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■ *As prevention in psychiatry really refers to early detection and consequent prevention of complications and chronicity, the general practitioner is the most important person in the medical community in preventing mental disorders. As more postgraduate courses in psychiatry become available to practicing family physicians, the majority of patients with psychiatric disorders will be effectively managed by the general medical practitioner.*

*The family physician is already doing this, although not as well as he could. In some instances, he may be unaware of the extent to which the disease with which he deals is psychic disease. As the number of community health centers increases, family physicians will play a vital role in their function. With the necessary knowledge to detect psychic disturbance and to treat emotional disorders effectively, the family physician will prevent many of the instances of progression to chronic psychiatric illness with which we are now plagued. The psychiatrist of the future will act as consultant, treating only patients with the more complicated mental disorders.*

THE FAMILY PHYSICIAN is the nation's greatest resource for the prevention and recognition of emotional disturbance. He is also the major treatment resource for psychiatric illness. From a nation-wide interview survey by the Joint Commission on Mental Illness and Health, a non-governmental multidisciplinary nonprofit organization representing a variety of national agencies concerned with mental health, it was reported in 1960 that 88 per cent of persons seeking help because they feared an impending "nervous breakdown" went to their family doctor. Only 4 per cent consulted a psychiatrist, while 3 per cent con-

sulted clergymen.<sup>5</sup> In other words, the general practitioner is the overwhelming choice of people who seek help for psychiatric problems.

One might ask what the treatment of incipient mental disorder, felt by the patient as an approaching "nervous breakdown," has to do with the prevention of mental disorder. Since this communication is concerned with the role of the general practitioner in prevention, it is appropriate to define prevention as it relates to psychiatric illness. In this connection, it is proposed to distinguish between two types of prevention: one, the promotion of healthy personalities capable of withstanding normal stress; the other, the early detection of developing mental illness. This paper will concern both aspects of the prevention of mental disorder.

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## The Concept of Prevention

Practically no one in psychiatry agrees with anyone else on how the healthy personality develops, or, indeed, on what constitutes a healthy personality. Most students in the field will agree to the rather broad statement that people are what they were to begin with, plus everything that happened to them after that. When it comes to assigning weight to the hereditary endowment, or the constitutional baseline, and to the various classes of events which occur after parturition, the general disagreement becomes manifest. It seems logical, though, that the relative importance of the many factors which act together to produce the final outcome of the personality, be it disordered or not, must vary in every instance. It seems equally logical, therefore, since little or nothing can be done, once birth has occurred, about modifying the hereditary or constitutional givens of the personality to direct prevention action toward the events, biological and interpersonal, that occur after the person is exposed to the world.

Susser and Watson<sup>9</sup> wrote: "The family is the reproductive nucleus of society, a fundamental social institution whose primary and essential task is to socialize 'the stream of new-born barbarians' so that they may take their place in life as mature and independent adults. From the moment a child is born the course of his physical and mental development is determined by his initial experiences within the family, and he can never free himself entirely from these early experiences. Every society, from nomads to city-dwellers, has the institution of marriage and stable family life. Through the family human beings maintain physical continuity by reproduction and maintain social and cultural continuity through training and education. The family regulates both the status and behaviour of the immature individual and controls his relations with other members of society."

The implications of the role of the family and of prevailing views on child-rearing are well illustrated in the following summary of Halliday's comments on differences between the child-rearing of many years ago and that of today (as quoted by Ewalt and Farnsworth<sup>4</sup>):

"Breast feeding was almost universal. In cases of difficulty, wet nurses were used. They were readily available, since about one infant in five died before reaching its first birthday. No special attention was paid to the length of breast feeding,

and the occasions of suckling were determined by the desires of the child or the mother. This was facilitated by the prolonged body contact between them, since the baby was carried about by the mother in the folds of a shawl. Carriages were the prerogative of the wealthy. At night the infant might sleep in a wooden rocking cradle, but often it lay alongside its parents or siblings. Such a practice often led to death from 'overlying,' especially if the parents were drunk, which was not rare in those days.

"Little bowel training was attempted until the second or third year. Infantile incontinence was of small moment to the generations who, before the introduction of water sanitation, possessed an easygoing tolerance of people's smells. Why worry? The child, given time, would naturally develop control of the sphincters and discover for himself the advantages of his unaided accomplishment. Floors were either stone or bare boarding, carpets being scarce and linoleum unknown. Furnishings were few but substantial; a table, a few wooden chairs or stools, and a straw bed often comprised all the furniture. The toddler had, therefore, a good deal of freedom, not only to defecate at his pleasure but also to explore and manipulate objects.

"The size of the family was large, children were plentiful, and juvenile nurses and playmates abounded. Toys were simple and few, and toddlers found natural pleasure in amusing themselves; hence, early social impulses found a ready fulfillment.

"Viewed physiologically, the child's environment was appallingly bad. Dirt, absence of pure water supply, inadequate sanitation, overcrowding, bad housing, poverty, malnutrition, and long working hours all contributed to tragically high rates of bodily impairments and death. Viewed psychologically, however, the child's environment was not so bad, for during the early years emotional growth was largely permitted to develop in its own way and in its own good time. The vital drives of the first and second phases obtained, therefore, a fair degree of outward expression; and it may be surmised that those physiologic dysfunctions and tensional states associated with the emotionally induced 'imbalance' of the vegetative nervous system were neither acutely provoked nor unduly prevalent. Only in the genital phase was there a great frustration of emotional growth; this took the form of ignoring the child, i.e., of seeing

him and not hearing him—a custom which, together with oedipal problems, may have a bearing on the apparently high incidence of hysteria in the Victorian era.

“Modern methods of child rearing have resulted in very great decreases in mortality and morbidity, but there are many rules and regulations, procedures to be followed, possible too-early bowel training, much emphasis on cleanliness, especially in view of the relatively abundant supply of household furnishings, carpets, bedding, etc. As a result of all the prohibitions, children have been set more and more against their parents, and the parents have felt that they are never let alone; the continuous reactive prohibitions and admonitions render the child inwardly insecure and outwardly difficult because of his inability to attain the orderliness, tidiness, punctuality, dutifulness, etc., demanded by the parents as a standard of behavior. Present-day life is apparently much more emotionally frustrating to children than that of the past.”

Additional studies on the role of early family life in the development of personality and in the genesis of personality disorders can be found in the works of Spitz<sup>8,9</sup> and of Bowlby.<sup>1</sup> Observations made by Spitz on infants in foundling homes who were denied close physical contact with mothering persons, and comparing the outcome of their personalities with those who were not denied this close contact gave us important evidence that such closeness and warmth in mothering is crucial to the development of the child in a healthy direction both physically and psychologically. In fact, children who are totally denied such contact fail to develop at all. Bowlby studied the behavior of children who were removed from the mother-figures to whom they were attached and placed with strangers. He advanced the thesis that once the child has formed a tie to a mother-figure, which has ordinarily occurred by the middle of the first year, rupture of that tie leads to separation anxiety and grief and sets in train processes of mourning. He further observed that in the early years of life, those mourning processes not infrequently took a course unfavorable to future personality development and proposed that they predisposed to psychiatric illness.

Once the child is out of the cradle, his personality is influenced by an increasing number of relationships outside the family. In all of these, the ability of the family to represent a constant, stable

and supportive force, while allowing the emerging individual to develop increasing independence from it, can make the difference between success or failure in the mastery of each successive stage of development. By the time the child reaches adolescence, if development has not been a healthy one, signs of personality disorder probably will be already in evidence. Since mental illness is a term now used to include everything from disturbances in one's way of dealing with others to major psychotic disorders, it is likely that the story has already been written by that time—mental illness, or mental health. Thus, prevention in the sense of averting the occurrence of mental disorder, must be closely related to the nature of the family life of an individual, whatever else it may be related to.

It should be emphasized, however, there are many variables in the formation of personality and in the production of mental illness. It is hard to know, therefore, whether or not even the most ideal family circumstances will necessarily prevent mental disorder. As a matter of fact, it is hard to define in our present state of knowledge exactly what “ideal” means when referring to family circumstances. There is some evidence that many things which at one time were considered to be deleterious to mental health and important in the production of mental illness, are actually not. For example, one study indicates that whether or not a mother works makes very little difference in the mental health of her children when they become adults. In fact, for the lowest and highest economic group, there is evidence that the children of mothers who work part-time had better mental health in adulthood than the children of non-working mothers.<sup>7</sup> The old notion about the effect of a broken home on mental health is now in question. A recent survey gives evidence that there is no greater risk of mental illness in a broken home than in one that remains unbroken, unless the remaining parent remarries.<sup>7</sup>

On the other hand, when one thinks of prevention as early detection of impending mental disorder, and instituting appropriate treatment to avert serious psychiatric illness, one is on a somewhat more solid footing. The signs of imminent psychiatric disorder are subtle but clear. They can be determined with reasonable accuracy and measures are now at hand which make it possible to take constructive action. If impending psychiatric illness is detected, and measures are taken to



preclude the necessity for treatment in a hospital, this is, indeed, prevention.

### The Role of the General Practitioner in Prevention

The classical role of the family physician in our culture has been changing in recent years. During the fabled Golden Age of Medicine, which may have existed at the beginning of the Twentieth Century for about 10 or 15 years, the family physician was friend, advisor, councilor and even ex-officio member of many family councils. Today, with our careful division of the members of the family, the mother has her gynecologist, the children have their pediatrician, the older members of the family have their internist, and recently the elders have begun consulting their own geriatrician. Now there is evidence of the appearance of a new specialty to deal with adolescents. It is becoming rather difficult for any physician to deal with the family as a unit. Nonetheless, there are a few encouraging signs of a return to the concept of family practice. The specialist may once again resume his role as consultant called in for special situations by a family physician who retains primary responsibility for the health of the family unit. Viewed from the standpoint of preventing mental disorder, this is a more appropriate function for the specialist.

The counseling of a mother in child-rearing, helping her to learn to cope with her conflicts and frustrations in relation to her child, is a natural and spontaneous development of the medical relationship. Somatic disturbances, which often reflect an element of tension in her life, present the ideal circumstances for such counseling. That same family physician, with appropriate training and adequate perceptiveness, could most easily detect early signs of disturbance in the family milieu, as reflected in the behavior of the parents and the children. The father, who for some reason seems to be ignored in most discussions of mental health and who is ordinarily the most difficult to involve in family counseling when it is indicated, would be much easier to work with if he too consulted the same family physician.

It is conceivable that the family physician can in time become a true resource for the prevention of mental disorder in the classical sense of the word "prevention." Recent sociological studies of the functioning of the family unit in health and in disease, as well as its relationship to larger socio-

logical units, are giving us information which can be directly applied by the physician who appreciates his role with the entire family. For example, physicians might well take active measures to change hospital policies which prevent parents from remaining with their children. The suggestion that the family physician concern himself with the functioning of the family unit assumes, of course, that he is willing to make himself acquainted with the available scientific information concerning family life. Continuing medical education programs now make such information available to family physicians.

There has been, however, a good deal of resistance by general practitioners to attending postgraduate courses and lectures given by psychiatrists on psychiatry in general practice. A recent course on "Sociology and the Family Doctor" offered to general practitioners in California had a total enrollment of 45 physicians out of 30,000 to whom brochures about the course were sent. This probably reflects a frequent complaint of many general practitioners that psychiatrists talk down to them and do not give them much useful information because they are afraid family physicians will either misunderstand or will attempt too much.<sup>6</sup> However, it may well be that enrollments for present continuing education programs in psychiatry are suffering from the errors of the past. There is considerable study going on now among postgraduate educators about the problem of defining teaching goals and developing teaching methods that will make psychiatric information available in useful form to practicing physicians. Psychiatrists hope to live down previous errors.

### Early Detection and Early Treatment

As indicated previously, the majority of patients with psychiatric disorders consult their family physician first. The family physician also treats most of the patients with mental disorder, if we include all psychiatric complications of somatic illness and all psychiatric illnesses which are manifested by somatic complaints. Few, if any, patients with the possible exception of those in the upper-middle and upper socioeconomic classes, see the psychiatrist as a useful or practical source of help.<sup>5</sup> Many patients with somatically manifested psychiatric disorders recognize only the somatic manifestation itself. Even if it were possible to persuade every patient who had a psychological disorder to see a psychiatrist, this would be neither feasible nor de-

sirable. The appropriate resource for early detection and early treatment is the family physician. Where he is not doing an adequate job of managing those patients, it is only because of lack of the appropriate skills and knowledge.

Caplan<sup>2</sup> described a number of practical steps that the family physician can take in helping to prevent emotional disorder. He pointed out that in addition to his role in safeguarding healthy relationships, in giving direct help in crises and steering people away from maladaptive solutions to interpersonal problems, the physician has an important role in the psychiatric consultation itself. That is to say, his responsibility is not ended when he calls in a psychiatric consultant. "Mental health consultation is a joint collaborative endeavor," Caplan said, "and what I meant to imply is that it has to be a two-way process, in which not only the psychiatrist but also the physician must be an active partner. It is essential for the physician to realize that he must take active steps to educate the psychiatrist during these consultations so that he will understand the special nature of the management problems involved, which will be quite different from what he is used to in the very unusual circumstances of his psychiatric clinic or office practice. Working with the same psychiatrist over a period of time, the physician may be able to teach him enough about the daily problems of general practice and the life situations of ordinary people who do not consider themselves psychiatric patients that he can eventually get answers which come reasonably close to being useful, but he will usually have to work quite actively to take what the psychiatrist has to offer and to translate it for his own use."

It is not generally appreciated, either by psychiatrists or nonpsychiatrists, that most of what psychiatry has to offer in medicine consists of skills and techniques that are part of the everyday medical relationship. For example in the average course on physical diagnosis, the second year medical student is given a long check-list of information to be elicited from his patient. He is rarely taught anything about *how* to elicit it. Yet psychiatric educators are constantly refining interview techniques so as to favor the emergence of a maximum of spontaneous information and a clear picture of the patient's psychological discomforts and usual interpersonal behavior. Similarly, what we have learned about the role of communication in the alleviation of psychological discomforts is

rarely brought out in courses relating to somatic disorder, although, of course, this is always emphasized in psychiatric courses.

The frequent separation of the psychiatric department from the remainder of the medical school or hospital contributes to a parallel compartmentalizing of the student's behavior toward patients. He learns one kind of behavior in the psychiatric department and a totally different kind in the rest of the medical curriculum. This splitting of his role persists into the practice years, and the average practitioner views "medical" behavior as separate and distinct from "psychiatric" behavior. One study reported that family physicians most often failed to diagnose psychotic conditions when these were accompanied by somatic complaints.<sup>3</sup> Yet with the effective integration of these two modes of behavior, the physician could effectively detect and deal with emotional disorders under the conditions, including time limits, imposed upon him by general medical practice.

Useful information about the newer psychopharmacological agents is available, yet rarely does it reach the family physician promptly. Far too often, the physician gets his information from the "detail man," who is essentially a salesman working for a pharmaceutical company, or from the striking and colorful advertisements in the medical journal, rather than from the articles and research reports in the body of the journal.

Unquestionably, need for treatment in a hospital can often be prevented through accurate diagnosis and early medication in the case of psychotic disorders. Equally often, prolonged psychiatric disability can be prevented by the appropriate diagnosis and interviewing techniques in patients who have minor somatic complaints of emotional origin. Similarly, patients with compensable injuries can be converted iatrogenically into chronic "compensation neurotics" by inappropriate handling.

## A View of the Future

I am going to make an optimistic prediction, based on my conviction that the medical practitioner must come to play an increasingly important role in the prevention and treatment of mental disorders. I will predict that in the years to come, the medical student will be taught psychiatry in its appropriate context—the medical ward and the medical clinic—and not in the psychiatric hospital and the separate psychiatric clinic. I will predict



that the newer kind of medical interview behavior which will result will be further reenforced during internship, residency training and postgraduate medical education. Thus, new medical interviewing techniques will permit the physician to deal with the whole patient rather than with isolated organ systems.

The medical practitioner of the future will deal with the entire family, medically and psychologically, having at his command resources that include consultants in specialty practices such as psychiatry. The role of the psychiatric consultant, as that of other consultants, will be to advise the family practitioner when asked to do so, and to treat only patients with complicated psychiatric disorders that are too time-consuming for the circumstances of family medical practice.

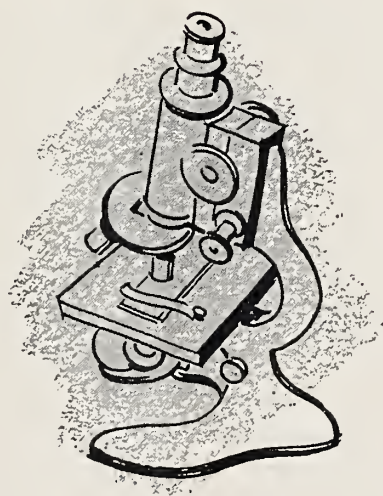
Family physicians will play a vital role in the function of community mental health centers, both in knowing how and when to make referrals to such centers and in contributing time to the actual functioning of such centers. With the necessary knowledge of sociological and other behavioral sciences, he will become a force for mental health in the community. With the necessary knowledge of how to detect psychic disease and how to treat emotional disorders effectively, the family physi-

cian will prevent many of the instances of progression to chronic psychiatric illness with which we are now plagued.

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# Aftercare of State Hospital Patients

## The Role of the General Practitioner

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■ *Of all the problems facing patients released from a state hospital, the most serious one is adjustment. Failure here means a return to the hospital. The present aftercare program of the Department of Mental Hygiene does not and is not intended to meet all of the patient's needs. It must rely upon other agencies to assist. It must rely upon the general practitioner to provide the continuity of care which is so important to successful rehabilitation.*

*The general practitioner can often make return to a state hospital unnecessary by an accurate assessment of the patient's problems, by effective intervention, by utilizing available consultation and by judicious referral. When services are not available, he can do much to make them available through the effective use of his professional channels.*

LAST YEAR there were about 27,000 admissions to the California state hospitals for the mentally ill, and more than 31,000 releases. Many of those released will be faced with a return to hospital in the future if they cannot make a satisfactory readjustment.

The management of this large number of persons in their post-hospital adjustment is an extensive problem. The inadequacy of present methods of management is reflected in the number of returns to the hospitals. The role of the general practitioner in the management of these patients varies considerably at present. Development of existing potential depends upon the image that the general practitioner has of himself and the value he ascribes to the services he has to offer the psychiatric patient. The value should be assessed in the light of the kinds of people requiring service, the

problems they face, what needs to be done and what facilities and services are available to do the job. Once the value is established, the role of the general practitioner depends upon how far he can extend his services. This, only he can decide. I will therefore attempt to define the scope of the problem, say what is now available and present some guidelines that may assist in making such an evaluation.

Who are the people being released from our state hospitals and what problems do they face? They have the normal everyday needs common to all of us. In addition, they have the problem of reestablishing themselves in a complex society. Some are children whose behavior had become so disturbed that their families and friends could no longer cope with them. Now, having been discharged from a hospital and still dependent on their parents, they must face a difficult readjustment period at home and at school, in addition to

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the normal stresses. Others are adults who, when they entered the hospital, left their home, job and friends behind. They now have to face an environment that has undergone change, just as *they* have undergone change. Still others are the elderly persons with concurrent physical disabilities. These physical problems add an even greater burden to the already serious emotional and social stresses they must face. Others may have specific problems such as alcoholism or dependence upon habit-forming medications. While they may have recovered from the toxic physiological effects, they still carry with them a latent emotional dependence that may again become overt as they have to face future stresses.

The nature of the patient's readjustment problem will vary with the length of stay in hospital.

When a person is released from a state hospital, he often finds himself in an unenviable position. Once the road to the state hospital is known, future trips can occur with less hesitation. Once a person has been in a hospital, returning to it can become the preferred alternative selected for him by others if he cannot conform to their expectations, regardless of how the patient himself may feel about it. This is true not only of relatives, but, unfortunately, of professional persons in his environment because this path may be more expedient. Instead of receiving assistance in meeting the additional problems of readjustment, the patient may face another admittance to hospital.

In reviewing some of the reasons for return to hospital, we often find that they are the same as those for which the patient was put in a hospital in the first place. While mental illness and emotional disturbances are not related solely to stress, it is useful to think in terms of psychiatric disorders as reflecting an individual's inability to cope with stress. Conversely, mental health may be considered a reflection of the individual's ability to cope with life stresses both external and internal. Symptoms of mental and emotional disorders, therefore, can be considered expressions of the person's attempts to deal with these stresses.

The state of decompensation that may result does not exist in a vacuum. The person is a social, psychological and biological member of a family and a community. Any change in his equilibrium disrupts not only himself, but also his family and community. When an individual's reactions become so extreme as to threaten the family or community, he may well become a candidate for

return to the hospital. But that may not be necessary if appropriate resources for alternative care and treatment are available. This would include all medical resources from the general practitioner to the local public or private psychiatric hospital. These resources must not only be generally available, but available to the patient when he needs them. A psychiatric clinic with a six months' waiting list may be across the street, but do him no good. Return to a hospital may then become the only avenue of treatment, despite the fact that he must again leave his family, job, friends and community.

Often the disturbance of equilibrium which the patient faces occurs not because of his inability to cope with normal stresses, but because of the added stresses his environment places upon him. In such circumstances, proper identification of the problem may reveal that family counselling, referral to a local welfare or employment agency, or referral to an attorney for domestic or civil matters is the desirable alternative to readmittance to the hospital or out-patient psychiatric treatment.

When a person can no longer maintain his social and emotional equilibrium, despite the assistance of available professional services, return to the state hospital is indicated. The decision to return will vary in accordance with the severity of the illness and with the medical resources available. If the patient resides in a metropolitan center, the decision may be different than if he resides in a rural area several hours away from the nearest medical facility.

Whenever return to a state hospital is indicated, there are certain factors that must be considered. Hospitalization in itself, whether in a state hospital or elsewhere, is but one step in the patient's treatment. The illness begins when the patient is at home. Treatment must begin there as well as end there. Just as with any other illness, hospitalization alone cannot be the answer. Just as with any other illness, continuity of care should start and terminate with the family physician. All too often, for many reasons, this is not the case today.

To be put in a state hospital is a severe dislocation of the patient from his environment. It is a rupture with his family and home. While absent, he must often maintain related responsibilities with little or no way of meeting them. It is a rupture with his occupation. He must take extended sick leave or perhaps an even more drastic step—resign and hope to obtain new employment on his

release. It is a rupture with the way of life which he has developed over many years.

To minimize the need for return to the hospital and to assist the patient in re-establishing himself, the California Department of Mental Hygiene has developed a program of aftercare services. Social casework follow-up is available through periodic visits and emergency contacts with psychiatric social workers in 27 field offices throughout the state. The patient can obtain assistance in meeting his employment, educational, financial and recreational needs as well as in working through specific emotional and interpersonal problems with which he may be confronted. Should the patient not have any social resources and be unable to care for himself without supervision, arrangements are made for appropriate foster care or nursing care and additional supervision as long as is needed. Medical follow-up is provided at each hospital through its aftercare facility. In major population centers a psychiatrist provides consultation to the Bureau of Social Work staff, and also gives medical supervision primarily to posthospital patients on tranquilizing medication.

To obtain maximum success in the rehabilitation of the mentally ill patient, services must be provided as early as possible, with as much continuity as possible, as close to home as possible and with as much social restoration as possible.

Continuity of care implies that the same key people remain involved throughout the patient's course of treatment. Multiple referrals confuse the patient besides duplicating and diffusing efforts and wasting valuable time. The first professional person called at the onset of an illness is usually the one with the broadest and most general knowledge, and, as such, is best qualified to provide the continuity of care. A logical priority then develops as to who should provide the patient with the appropriate care and treatment. First priority is the private practitioner; local private or public agencies the second; state agencies the third.

The Department of Mental Hygiene's follow-up program is a third priority service, although often used as a first priority service. These follow-up services provide much-needed support to the patient who has no other available resources. These services are limited, are not intended for indefinite care and are established to fill an important gap. They cannot provide the intense, individual, total medical care that is the province of the general practitioner.

Where the general practitioner is available, either through his services to the patient or the family, he becomes the key person to provide the medical follow-up. Having the trust and confidence of the family and patient, and being the most easily available medically responsible person, he significantly influences how early the patient receives treatment, how much continuity of care is given, how much dislocation from his home the patient is to endure, and eventually how much social restoration is possible.

In the final sense the general practitioner can determine the success of rehabilitation.

It may well be time for the general practitioner to reassess the value of his services to the psychiatric patient. The management of the post-hospital patient provides an unequalled opportunity to do this. Although the patient has had a psychiatric disorder, there has been, as well, enough remission in the symptoms that he is ready to reestablish himself in his previous environment. Records are available of his illness, his treatment and his course in the hospital. Consultation is available for the future management of emotional problems.

In the management of the post-hospital patient, just as with any patient being treated for a psychiatric disorder, there are four factors to consider: Identification of the problem, intervention, consultation and referral.

1. *Identification of the Problem.* The patient must be assessed as a biological, psychological and social entity. Problems occurring in one area give rise to concomitant problems in others. Any diagnosis that is made should take into consideration the physical, emotional and social factors. It should, as well, clearly identify the nature of these components, the extent to which they are affected as well as the manner in which they are inter-related.

A thorough diagnostic work-up in the aged is of particular importance. An accurate identification of the problem areas is the first step in preventing a return to the hospital.

2. *Intervention.* Maintaining the physical health of the patient and correcting any physical disease is an important factor in successful rehabilitation. The confusion, apathy, disorientation and agitated behavior found in elderly persons are symptoms that often lead to psychiatric hospitalization. These symptoms often have their origin in correctable physical disease. Treatment of diabetes or of cardiac failure, reassessment of medication or reevaluation of diet can often control these



symptoms well enough that return to a state hospital becomes unnecessary.

Should admittance to hospital become indicated, treatment of the patient in a general hospital near his home may be a far better solution than return to a state hospital. This holds true not only for the elderly, but also, for example, for alcoholics. Detoxification need not take place in a state hospital. It could just as well be achieved in the local general hospital if it is available for the purpose.

Management of emotional problems need not always require the services of a specialist. The appropriate use of psychotropic medication and realistic support can do much in helping a person cope with existing stresses or face additional stress, or eliminate stress that may be detrimental. Recognizing the patient's problem and his reactions to them, allowing him to unburden himself of his fears and anxieties, and helping him to obtain perspective about the possible ways in which he can cope with stress are not tools just limited to the specialist. They are an important part of the everyday armamentarium of the general practitioner. The support of realistic reassurance and helping the patient utilize the healthy aspects of his personality cannot be underestimated in assisting him to achieve stability with his environment. Of particular importance in the patient released from a state hospital is seeing that other people in his immediate environment have a realistic image of the patient and their relationship to him. This is just as important as the necessity that the patient have a realistic image of himself and others. This means not only working with the patient but often with his family as well.

Helping the family relieve their own anxieties and fears about the patient can do much to prevent an additional unnecessary burden being placed upon him and perhaps another hospitalization.

3. *Consultation.* To the physician, effective use of the specialist's consultation is often the difference between continuing with the management of the patient and referring him to another resource. To the patient it often means the difference between receiving his treatment from someone he knows and trusts and having to face another stranger or group of strangers, go through another evaluation and assessment and develop another treatment relationship. To the post-state hospital patient it often means the difference between stay-

ing in his community or returning to the hospital.

Providing direct services to post-hospital patients, who can get no other services, has been a function of the Department of Mental Hygiene's after-care program. Consultation to the general practitioner as a part of this service is even now available from the hospital, its aftercare facilities, and its psychiatrists in major population centers. Information about the patient's social adjustment and about community agencies which may be considered potential referral resources is available from the Bureau of Social Work offices. The availability and effective use of these consultation and information services may well make the difference between the patient's making a successful readjustment and returning to the hospital.

4. *Referral.* The need for basic or more specialized services, either as an alternative to present care, or as a component of a multiphasic approach to the patient, constitutes the major reason for referral.

These services may be in the realm of intensive psychiatric intervention. They may also be such services as those required to meet the patient's educational, employment, recreational, financial, or residential needs.

Judicious referrals are a help to the patient; unnecessary referrals confuse him, irritate him and waste time. The safest approach to an effective referral is through appropriate consultation. Specific and effective referrals can be made, through the use of state agency offices such as the Department of Mental Hygiene facilities previously mentioned, and the use of local community mental health agencies and programs.

The most important element of the referral, however, is the fact that the patient, while receiving the specialized services, should remain the physician's patient. If the patient must leave the community and return to a state hospital, the major link which can assure any continuity of care is his family physician.

Should the needed services not be available, then the physician has another responsibility. Through the professional channels available to him, he should make his needs known and participate in planning and developing the services that are needed.

This is a joint responsibility that we have to facilitate our treatment efforts and most of all to protect the patient's welfare.

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# The Troubled Adolescent Patient

## How the General Practitioner May Be Helpful

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■ *The disturbed adolescent is psychologically isolated from the worlds of childhood and adulthood. His sense of alienation results from both the upsurge of instinctual drives and his uneasy attempts to master changing physical attributes and new freedoms and responsibilities. The former result in conformity and in concerns about "normality." The latter lead to confusion and to alternating rebellion and over-dependence.*

*The general practitioner may be the first person consulted by the troubled adolescent or his parents. The physician's sensitivity can be crucial in helping the family work together toward a solution. Persistent anxiety in either parent or child is in itself a problem. An understanding of those factors inherent in the adolescent experience may provide the physician with a recognition of disturbance denied by the adolescent with a facade of bravado or indifference.*

*The physician must be prepared to help the adolescent accept a protracted period of stress, usually with only partial resolution of distressing problems.*

ADOLESCENCE is that period of life spanning the transition from childhood to adulthood. Most youngsters, inspired by the new and broadening challenge of their lives, and with the help of understanding adults, flourish during adolescence. For them the teens and early twenties are recalled later as among the best years of their lives. Yet in our society increasing concern has developed about the large numbers of young people who pass through these years without grace and achievement, remaining troubled and immature and con-

tributing neither to their own nor to the general welfare. Many adolescents experience a degree of inner turmoil leading to overt symptoms of disorder, including serious antisocial behavior.

It is these troubled adolescents who, presenting problems to themselves, their parents and society, come to the special attention of physicians generally and who may be seen by psychiatrists. In this presentation, it will be possible to examine only briefly some of the psychological and physiological problems of the adolescent and certain parental and social factors which influence his adaptation. The most characteristic modes of symptomatic expression of disturbance among

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adolescents will be discussed and attention will be given not only to ways in which physicians may be helpful but also to factors which may limit the physician's helpfulness to adolescents and their parents.

### Impact of Puberty

The disturbed adolescent feels psychologically isolated from the worlds of childhood and adulthood as he uneasily attempts to master changing physical and psychological attributes.

Anxiety may be aroused in the adolescent by the intensification of quiescent conflicts preexisting from earlier experience, not just about genital sexuality but about multiple sources of gratification. These may be related to eating and to concerns about bodily contact. They may accompany extremes in behavior with regard to body cleanliness, having antecedents in clashes with parental authority. Such conflicts may revolve around the use of the body as a whole, including kinesthetic pleasures and athletic prowess. In all these areas, the adaptations that "worked" in the past may no longer be successful.

In addition, as the physical capacities and energy of the youngster increase, so must his ability to channel and utilize these capacities. Coincident with the task of mastery of new awareness of and new information about himself and the world, the adolescent must deal with added freedoms and responsibilities. Both are demanded by the youngster himself and expected of him by others. The adolescent frequently wants more freedom and less responsibility than either his parents or the community will extend to him.

### Parental and Social Factors

Parents bring to their relationship with their children vestiges of their own unresolved conflicts as well as the wish to protect their children from their own mistakes or from others witnessed or imagined. Because a child necessarily represents part of the parents' own achievement, most parents have an emotional investment in the success of their children that is closely tied to their own self-esteem.

Parent and child alike live in a rapidly changing world. Altering concepts of effective economic, sociological, and international policy sharply threaten the status quo, the equilibrium of the past. We are witnessing the increasing dissolution

of family ties, the waning of traditional mores, and the widespread failure of religion to meet the needs of man for a stabilizing ideology. At the same time, through welfare and public help programs we are utilizing resources increasingly for humanistic goals. In their anxious resistance to this dichotomy of forces leading to such broad changes in our society, many adults take refuge in positions of reaction and rigidity. The adolescent may be more ready to accommodate to the requirements of the emerging new order than are his parents. The challenge of authority by the adolescent then presents the parent with both the ultimate threat to his sense of personal worth and the temptation to battle. By restraining the adolescent's behavior the parent may hope to demonstrate to himself mastery of his own uncertain and conflicted feelings.

### Social Pressures and Peer Groups

To the extent that goals of excellence are perceived as out of reach, or attainable at too high a price to an adolescent, he must dissociate himself from involvement. To the extent that his immediate constellation of elders themselves appear ignorant, confused or in a paralyzing state of conflict about social and economic problems, the adolescent may perceive himself as even less adequate for successful involvement in the struggle. Finding models for a personal ideology more often than not fragmented and blurred in our culture, he may rely more than ever for his sense of personal integrity and worth on identification with his peer group.

As the adolescent seeks acceptance from his peers through conformity to group standards as he perceives them, he is particularly concerned with what is "normal." Confusion about which attributes may be regarded as masculine or feminine reflects universal conflicts arising in the effort of each individual to achieve a sense of sexual identification in early childhood. The adolescent must come to terms with his intensified conflict about sexual expression in one of several ways. He may decline to accept an "adult" sexual role, finding an outlet in masturbation, in a relationship with a member of his own sex, in asexuality or in fantasy alone. He may find peer group support and sanction for active heterosexual behavior. He may largely sublimate and redirect his energies into intellectual pursuit or physical activities. Most adolescents utilize several of these ways of meet-

ing their own needs at different times and in differing degrees.

### Physiological Problems

The concern about "normality," intensified by his struggle for sexual identity, creates genuine distress for the adolescent with any of the physiological problems so often encountered among the pubescent. One such common problem is that of delayed physical maturation, whether expressed by late appearance of secondary sexual characteristics or by delayed growth of stature and physical prowess. Less often recognized is the distress of the youngster with precocious puberty, whose physical and psychological growth precedes that of his contemporaries. Such a youngster initially will be advanced in stature and intellectual skills, only to find himself relatively smaller in stature as others mature. Anxiety about his intensified instinctual life may be pronounced, since his social and life experience have not yet prepared him adequately for its integrated acceptance. At either extreme, when the timing of physical maturity does not parallel that of his peers, the youngster invariably feels "different" and hence, often, "inferior." Other physiological problems disturbing to adolescents and commonplace in the experience of general physicians include obesity, acne, hypogonadism, and various physical anomalies, particularly those involving the reproductive system.

### Psychiatric Disorders

It has been possible here only briefly to characterize the adolescent experience in its psychological, sociological and physiological aspects. The typical adolescent can be seen as earnest and eager for new experience, while often anxious and confused about his capacity to achieve. He is concerned about his own worth, his identity as a sexual being and his acceptance within the peer group. While seeking acceptance and reassurance from adults, he is alternately rebellious and overdependent.

Symptoms of disturbance in the adolescent may range from caricatures of these prototypical adjustment patterns to the more disruptive problems of delinquency, depression or psychosis. The anxious adolescent may seek help with problems he has been unable to discuss at home. The most widely recognized source of anxiety and guilt among adolescents is masturbation. Similar con-

cerns about homosexual impulses and about heterosexual experimentation may lead a youngster to seek help. Such open concern is, of course, easier to meet than more covert or unconscious anxiety that seeks symptomatic expression.

Since many children grow up being taught to feel guilty about the expression of their own impulses, they learn to perceive themselves as basically bad. When, as adolescents, their energy becomes increasingly utilized in defense against these impulses, they may have little capacity left to expend upon external success. This leads to failure at school or in living with others, and reinforces feelings of worthlessness. The adolescent may react by withdrawing from competitive effort. He may feel lonely and misunderstood, finding isolation from contact with adults and peers alike preferable to the rejection he feels from others. In this situation, he is likely to retreat into fantasies that express forbidden wishes and in which he achieves the success not experienced in actuality. Depressive reactions, including those leading to suicide attempts, may ensue, particularly in the face of crisis. Other adolescents direct their energies more successfully into constructive intellectual pursuits, yet remain personally unhappy and unsuccessful in interpersonal relationships.

In response to anxiety about their emerging feelings, or to concern about their adequacy to compete successfully in the adolescent world, some youngsters try to deny their changing status. They seek in many ways to perpetuate and extend their state of dependence upon their parents. Usually parents of such children have subtly fostered the dependent state of the child and are themselves unconsciously reluctant to give up that relationship. The ambivalence of these parents is often expressed in equally intense concerns about the failures of their children to develop self-direction and a sense of responsibility. The parents' resulting anxiety may lead to genuine hostility toward the child. Parent and child become mutually skillful in manipulating and controlling each other when the equilibrium is threatened. Often, because such a balance is based upon hurt as well as gratification, there are repeated crises and a multiplicity of psychoneurotic or psychosomatic symptoms in both parent and child. Such a youngster seeks younger children or adults for companionship, for he provokes contempt and open rejection from his peers.



The denial or the inhibition of impulse may not be successful defenses against anxiety under the impact of puberty. One regularly sees adolescents expressing various conflicts by forming a compensatory reaction against forbidden or feared aspects of their instinctual life. Concerns about being dirty, therefore bad, may be expressed not only by obsessive concerns about cleanliness. They may be observed in the opposite behavior, as in insistence upon the right to be dirty. Similarly, it is the adolescent most fearful of his own repressed homosexual impulses and the danger of their expression who will be the most righteous about interpreting behavior of others as "queer."

It is hardly surprising, in view of the multiplicity of problems to be met by the adolescent, that among his peers the successful rebel is generally admired. Here is a person apparently confident of himself, free to be aggressive, and offering leadership in challenging the ambivalently feared and respected but contradictory society of the adult. While recognizing such rebellious feelings as characteristic of adolescence, adults often view rebellious behavior as delinquent. Increasingly psychiatrists are recognizing the presence of neurotic conflict behind truly delinquent behavior. With the recognition formulated in the psychiatric literature as recently as 1952 that children often express in antisocial behavior the unconscious wishes of their parents, programs for the treatment of delinquents have tended to include treatment of their parents.

The adolescent seemingly most indifferent about adhering to accepted behavior patterns is often hungry for attention and acceptance. He may have developed very little inner capacity for self-control. This occurs because his parents have themselves been in conflict about setting limits upon his behavior and thus in helping him to learn discriminating ways of achieving satisfaction. Such a youngster becomes increasingly anxious about control, constantly testing the adults around him for their response. Having given up hope for affectionate and considerate help from others, he may manipulate and insist upon control of situations and relationships as a means of reassuring himself that he can provide the control he needs. In doing so, he further alienates those from whom he might expect most help. Then, feeling more alone and anxious, he may engage in increasingly more delinquent behavior until restrained by legal authorities.

The psychosis now described as a schizophrenic reaction was first named "dementia praecox" because of its frequent onset in youth. It should be noted, however, that other conditions may be mistakenly called schizophrenia, sometimes leading to hastily arranged entry into a hospital—traumatic for the adolescent. Particularly common among adolescent girls is a dissociative reaction, acute in onset and brief in duration, in response to a specific stress. This has often been called "hysteria" and is not accompanied by the thought disorder of psychosis. Although toxic states from drugs or alcohol may not be recognized as such at first, the cause can generally be identified by careful history taking and by the noting of defects in the sensorium that are not present in the functional psychoses.

### The Role of the Physician

An understanding of these characteristics of the adolescent experience and of the more typical expressions of maladaptation in the adolescent will help the physician in work with such patients. However, learning to be accessible to troubled young people may remain difficult. The required time and patience are hard to maintain in the busy schedule of many practitioners. Especially difficult for many of us to develop is sensitivity about the ways adolescents communicate about themselves and of their usually great reluctance to openly acknowledge problems to adults. The physician's skill in helping a youthful patient overcome this reluctance can be particularly important since the physician may be the first person consulted by the troubled adolescent or his parents.

The adolescent may be brought to the physician by his parents because of their concern about his adjustment or for ill-defined malaise and physical complaints. The adolescent may be unaware himself of the extent to which his problems result from inner turmoil. Shame about his own impulses or behavior may be restricting his openness. The need felt to deny all difficulty in the absence of assurance that he will be accepted and understood may be primary. If his listless lack of communication provokes impatience or criticism, he may be even less able to acknowledge his distress.

Other youngsters may openly bid for attention and a confidential relationship while persistently avoiding discussion of real concerns. Often the manifest content of their talk only serves to mask consciously felt difficulties. For instance a boy may

attribute his problems to lack of athletic skill while actually being more deeply concerned about a felt rejection from his parents or perhaps anxiety about his own sexual impulses considered by him to be "abnormal." An increase in physical tension evident when certain topics are discussed may be the only clue about carefully guarded concerns. Obvious omissions or casually expressed afterthoughts may point more cogently than lengthy exposition to areas of deeply felt anxiety.

In his need to deny anxiety both about his own impulses and the threat felt from others, the adolescent may present an air of bravado and indifference. This may be particularly exasperating to the physician who, aware of a youngster's genuine problems with society, may be convinced that reaching the patient is hopeless. When, in such a situation, a physician attempts abruptly to unmask the denial, his patient may become acutely anxious and avoid all further communication.

It is difficult to emphasize enough the value to the adolescent of the adult who can be accepting and non-judgmental while attentive to whatever communication, both verbal and non-verbal, may be forthcoming. Criticism, admonition, and advice are commonplace in the experience of these young people. Indifference, dismissal, or helpless dismay are equally confounding. Reassurance may not only be valueless, but in itself may seem a dismissal. Therefore the interest and availability of an adult with an understanding and accepting attitude can be tremendously therapeutic.

In assessing the situation of a given youthful patient, the history of difficulty is of course important. If this includes the perceptions of both the child and his parents, so much the better. There may be instances when the youth alone is available, or when he insists that his parents not be consulted. In the latter instance it is sometimes possible to effectively convince the patient that contact with his parents is important, since helping them understand their part in the patient's problems is a way of helping him. Valuable in the understanding of any crisis is data about its timing, about significant events preceding its onset, and their effect upon not only the patient but his family. Significant details may be dismissed by the informant as irrelevant or unimportant. Brief and alert exploration of the immediate or chronic difficulty will enable the physician to evaluate the accessibility of the patient

and his family for help, their capacity and motivation for working through a crisis, and usually an indication of whether further help will be needed.

Since parent or child may only seek help at a point of deep discouragement, a readiness on the part of the physician to become engaged with them in seeking constructive paths toward resolution of problems can in itself encourage renewed effort. Often misinformation about pubescence itself, or distorted perceptions or expectations in the adolescent or his parents can be brought to light. These may then be reexamined by each concerned, with facts clarified and working through of misperceptions begun. As an understanding, respected and uninvolved person, the physician may bring to the attention of the adolescent patient or his parents alternative choices to those courses of action taken in the past. While direct advice is seldom useful when at odds with the feelings of the recipient, he may feel freer and more encouraged by consideration of such possible alternatives.

When any person avoids direct discussion of topics considered unacceptable or shameful, the unanxious and direct capacity of another to broach the subject can be experienced with genuine relief. Thus by demonstrating an awareness of common adolescent concerns, with a wish to understand the particular person involved, the physician may foster greater openness about problems on the part of his patient. Such conversational and inquiring discussion may be possible even in the absence of specific clues about the adolescent's special problem. However, persistent probing about suspected areas of conflict may prove threatening to him and disruptive to work with him.

Persistent anxiety in either parent or child is in itself evidence of situational stress or chronic neurotic conflict. There are times when helping the anxious parent of an adolescent evaluate the parent's own distress which may have gained a focus in the behavior of the adolescent is more helpful than directly dealing with the child. This may free the parent himself to be more helpful to his youngster. There has been an emphasis in this discussion upon the interaction of family members because of the conviction that emotional problems generally arise in the setting of interpersonal relationships. Certainly there are adolescents, particularly in the late teens and older, who may function with considerable independence as



regards the family. With these patients there may be less need to involve family members.

Few human beings, including psychiatrists, are without some residuals of unresolved neurotic conflict. As a former adolescent, and often as a parent of adolescents, the physician needs to maintain an awareness of his own feelings aroused by confrontation with a given adolescent and his problems. The physician, like the parents, may unconsciously deal with a child not with understanding and with a readiness to be helpful. He may instead feel the same sense of threat and temptation as the parent. He will then respond not only to the child but also to his own anxieties and their derivatives in attitude and behavior. Respect for the confidentiality of his relationship with the adolescent is essential, although the physician needs to remain clear with the youth about his ethical obligation to the legally responsible parents. He may be able to encourage the adolescent himself to be more direct with his parents.

The physician will be unable to help all adolescents who come to him. Certainly an impatient hope that quick solutions are always available will be met by disappointment. Many physicians have found it useful to discuss the problems of their patients with a psychiatric colleague as an aid in planning a successful intervention of their own

with a given patient. When it is not possible to come to an understanding with a family about the nature of their crisis, or when persistent difficulties indicate a need for continuing help, psychiatric referral may be indicated.

Fortunately, adolescence is not a time of problems alone. It is also a time of exciting discovery and opportunity. Youth is characterized by resilience and energy. Growth and maturation is a continuing process. Therefore, time and increasing experience in themselves will equip the adolescent with greater capacities for dealing in integrated fashion with both inner and external tensions. Meanwhile, we must be prepared to help the adolescent find solutions for individual crises and help him to accept a protracted period of stress, usually with only partial resolution of distressing problems. Successful negotiation of the storms of adolescence may be particularly difficult at this time in the evolution of our society. Children and adults alike live under conditions of change and threat to the established order, indeed to the preservation of life on earth as we know it. Therefore, the need to adapt to prolonged stress characterizes not only the life of adolescents, but is a concomitant of life in our time for all human beings.

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# Pigmented Nevii

## Induced Changes in the Junctional Component

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■ *The pigmented nevus represents a potentially more dynamic lesion than has been indicated by most published studies. New nevus cell clusters frequently appear in the epidermis over the residual portion of a nevus that remains after partial surgical excision. Even in relatively inactive nevi in adults, new junctional nevus cells may be induced by surgical trauma. This stimulated growth usually regresses by the time one year or more has elapsed. The growth of nevus cells is probably comparable to that induced in other cells by traumatic injury. There is no evidence to suggest that it is related to the development of melanoma in pigmented nevi.*

PIGMENTED NEVI may grow during the course of their development. During the growing period one usually finds nevus cells in the epidermis as junctional foci, so-called because of their location at the dermal-epidermal junction. These intra-epidermal cells are commonly viewed as an expression of growth activity, but the identification of multiplication of these cells is difficult.

Several reports have indicated that new epidermal nevus cell foci may appear after surgical planing or other excision of the surface of certain nevi.<sup>3,5,6,7,8</sup> Most of these lesions have been in children and with one exception<sup>6</sup> those where a preliminary histological study was made have presented junctional foci at the time of the initial operation. Our investigations<sup>2</sup> have indicated that junctional activity may be induced commonly, even in intradermal nevi, as a sequel to superficial partial surgical excision followed by light electrodesiccation.

This finding was derived from the examination of 143 intradermal or compound nevi from 103 patients, 85 of whom were beyond the age of 20. The superficially excised portion was examined histologically and the lesions were divided into three classes on the basis of the character of the junctional component. Class 1 represented the intradermal nevi, including those with occasional

small epidermal foci of the sort that can be found in many intradermal nevi on serial sectioning.<sup>4</sup> Class 2 and Class 3 exhibited moderate and marked junctional activity respectively. Subsequent biopsy specimens from the same lesions were removed from one month to six years later. Forty-four showed only scar tissue, leaving 99 residual nevi, which were compared with the corresponding initial biopsy specimens.

The study showed that the regenerated epidermis over the residual intradermal portion of partly excised nevi frequently contained nevus cells in clusters duplicating those of the intra-epidermal portion of untreated compound nevi (Figure 1). In some lesions this represented a return of a junctional component, often in an exaggerated form, following partial excision of an initially compound nevus. In 34 instances there was a development of prominent intra-epidermal changes when the original lesion had been classed as an essentially intradermal nevus. (Figure 2). In most of these cases re-biopsy was done within 12 months after the partial excision (Table 1). In this group 68 per cent of the lesions that originally were Class 1 had become lesions of Class 2 or Class 3. Although the entire covering epidermis had been removed from the lesions which were initially Class 2 and Class 3, each of these, upon re-biopsy within one year, showed a regrowth of epidermal nevus cells, and the lesions remained as compound nevi.

The earliest reformation of intra-epidermal nevus

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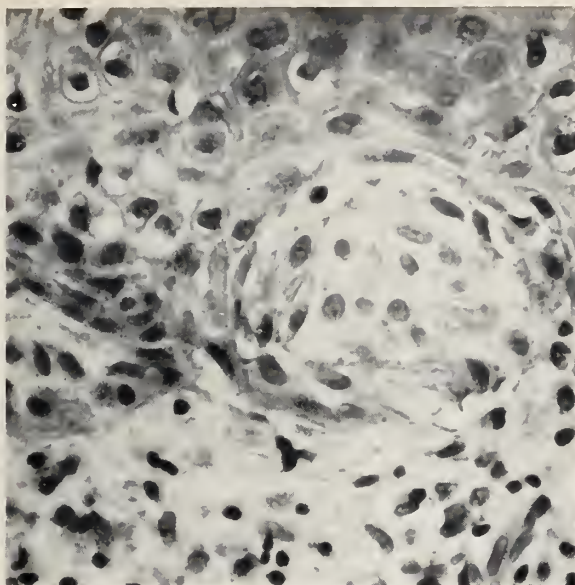


Figure 1.—Pigmented nevus cell cluster in regenerated epidermis three months after partial surgical excision of a nevus that showed no junctional activity in the initial specimen (Hematoxylin and eosin stain×600).

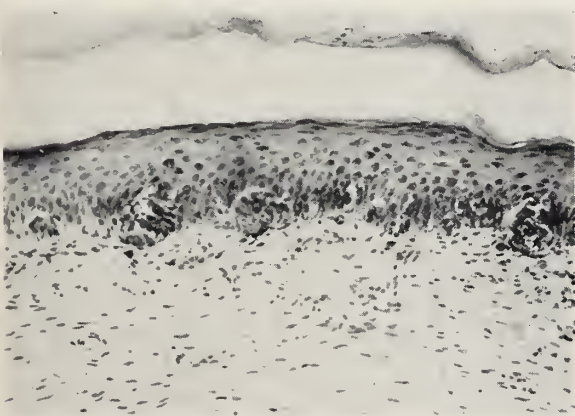


Figure 2.—Many small intra-epidermal nevus cell clusters and heavy pigmentation of the basal epidermal cells present one month after partial excision of a nevus that was initially intradermal. A prominent scar separates the newly formed junctional component from the dermal residue, which is not included in the photograph (Hematoxylin and eosin stain×140).

cells was seen in two specimens removed one month following the initial surgery. Similar induction of new intra-epidermal nevus cells, which were frequently more prominent than those of the initial specimens, occurred in five lesions after six weeks, and in 12 lesions after two months.

When the excision of nevus residues was carried out more than one year after the initial operation, however, a different situation was encountered (Table 2). Here approximately three-fourths of the persistent lesions showed inconspicuous junctional activity, and only one instance of marked intra-epidermal nevus cell growth was ob-

TABLE 1.—*Junctional Change Over Residual Nevus After Partial Surgical Excision (Lesions Studied Within One Year)*

Status at Original Biopsy	Number of Lesions	Status at Second Biopsy (Per Cent of Lesions)		
		Class 1	Class 2	Class 3
Class 1.....	41	32%	44%	24%
Class 2.....	17	....	71%	29%
Class 3.....	6	....	33%	67%

For definition of classes, see text.

served. In the latter case the second biopsy was performed only thirteen and a half months after the initial partial excision.

These findings indicate that junctional activity in a nevus may be induced by appropriate means but that this growth is usually transient. Whether stimuli other than surgical trauma may evoke similar growth in nevi has not been tested, but the possibility is apparent that the natural history of some intact nevi may include episodes of increased growth of the epidermal component even after the structure of an intradermal nevus has been attained.

## Discussion

These observations have not identified with certainty the source of the induced epidermal nevus cells. Although the great majority of such cells had been removed with the initial biopsy specimen, it is possible that a few residual foci in the surrounding epidermis or in remaining hair follicles served as the source of new nevus cells in the repaired epidermis. One cannot exclude entirely the suggestion of Schreus<sup>7</sup> that dermal nevus cells grew into the newly formed epidermis, particularly since a role of residual intradermal nevus cells appears to be an important aspect of the process which led to the appearance of junctional activity over residual nevi.

With three exceptions, intradermal nevus cells were always found whenever intra-epidermal nevus cells appeared in re-biopsy specimens. In two of the exceptions the specimen for study was sufficiently thin so that it may not have reached deeplying residual nevus cells. The dermal nevus remnant was frequently separated from the epidermis,

TABLE 2.—*Junctional Change Over Residual Nevus After Partial Surgical Excision (Lesions Studied After More Than One Year)*

Status at Original Biopsy	Number of Lesions	Status at Second Biopsy (Per Cent of Lesions)		
		Class 1	Class 2	Class 3
Class 1.....	24	75%	25%	....
Class 2.....	7	86%	....	14%
Class 3.....	4	25%	75%	....

For definition of classes, see text.



however, by a layer of scar tissue up to 1 mm thick, and there was no morphological evidence of migration of nevus cells from the residual dermal component. A final possibility is that the new nevus cells were derived from melanocytes in the regenerated epidermis. This would imply some special stimulatory mechanism, presumably related to the intradermal nevus cells.

Regardless of the origin of the new intra-epidermal nevus cells, it should not be surprising that they proliferated after trauma. Epidermal cells are often stimulated to rapid growth by trauma, and melanocytes have been shown to proliferate in association with regenerating epidermis.<sup>1</sup> If the nevus cells or their precursors possess any growth capacity comparable to that of melanocytes, this might be expected to be exaggerated as part of the active growth of all epidermal elements during repair.

Although the nature of the apparent influence of the dermal nevus remnant upon the induction of junctional nevus cell proliferation remains undetermined, the findings under discussion emphasize the relationship between the epidermal and dermal portions of nevi and speak against any basic qualitative differences between the common types of pigmented nevi.

An important question is whether traumatic stimulation of epidermal nevus cell growth relates in any way to the development of melanoma. There is no more reason *a priori* to believe that this should be the case than to expect squamous cell carcinoma to form in the regenerating epidermis over a wound. A great deal has been written, however, about the possibility of malignant transformation of nevi by trauma, and conflicting opinions have evolved. Our belief, supported by the absence of histological evidence of malignant change in any of more than 200 biopsy specimens obtained at different intervals following partial excision of nevi, is that surgical trauma does not induce melanoma. We have been unable to find any reported instance of melanoma that appeared at the site of a partially excised nevus after the removed portion had been found free from melanoma by adequate histological examination. Although we do not regard partial excision of benign nevi as dangerous, we emphasize the importance of histological examination of the excised portion of such nevi to insure that the lesions are indeed benign.

Another question relative to this study is whether

recognition of the phenomenon of epidermal nevus cell regrowth has practical value. While its principal value is its contribution to understanding of the nature of pigmented nevi, appreciation of the nature of the stimulated junctional activity and its course may aid in the management of cases after partial excision of nevi. Local pigmentation appears frequently at the site of partially excised nevi, and this may be a source of worry unless it is recognized that, like the frequently associated regrowth of epidermal nevus cells, post-traumatic local pigment deposition in the basal layer of the epidermis over residual nevi appears early and decreases with the passage of time. In about half of the residual nevi which we have examined within one year, histological sections have shown more pigment in the regenerated epidermis than in that over the original lesion. After more than one year, however, only 9 per cent retained such increased epidermal pigment. This suggests that there is no cause for alarm if the skin over a partially excised nevus becomes prominently pigmented.

More extensive observations will be necessary to determine whether the ultimate regression of the epidermal component of nevi after partial excision is as great as that in untreated nevi, but since 88 per cent of the nevi in our series that were examined more than one year after partial excision had no recognizably greater junctional activity than was manifest in the original nevus, it seems highly probable that after several years the difference in junctional activity between treated and untreated nevi will be negligible.

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# Radiographic Diagnosis of Intestinal Perforation in Early Infancy

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■ *Records of 25 patients with intestinal perforation in early infancy that were treated at the Los Angeles County General Hospital in a period of 15 years were reviewed. Sixteen had roentgen evidence of pneumoperitoneum, and nine did not. The mortality rate was 94 per cent in the group with pneumoperitoneum, 78 per cent in the other, and 88 per cent overall. Multiple sites in the gastrointestinal tract were involved, and the causes of the lesions were diverse and frequently obscure. Prematurity, obstetrical and iatrogenic complications, and congenital anomalies were factors often associated with intestinal perforation. Roentgen features appeared to offer the best hope for diagnosis and appropriate treatment.*

INTESTINAL PERFORATION is a serious condition at any age, but especially so in the young infant. The cause of many perforations in this age group is poorly understood. Anoxia with intestinal ischemia, unrecognized trauma and congenital smooth muscle defects in intestinal wall have been suggested.<sup>1,5,10,11,15</sup> In most instances it is difficult or impossible to ascribe a specific cause.

We have observed 25 cases of intestinal perforation in early infancy at the Los Angeles County General Hospital over the past 15 years. Of these, 16 had roentgen evidence of pneumoperitoneum and nine did not. The clinical signs of intestinal rupture in infants are nonspecific, and frequently the symptoms are those of respiratory distress or septicemia. The physical findings are usually abdominal distention, tachypnea, vomiting and obtundation. Clinical diagnosis is usually late. Radio-

graphic evaluation is helpful in early diagnosis if ileus or intraperitoneal fluid or air is detected.

In the group with pneumoperitoneum, most of the cases occurred in the first week of life (Table 1). The group of patients without pneumoperitoneum had no apparent peak incidence. There were 14 males to 11 females in both groups combined, and this does not appear to be a significant sex difference. Similarly with regard to racial differences, there were 15 Caucasians and 10 non-Caucasians in the groups combined. Because of the small number of cases, and the type of population sampled at this hospital, we do not feel that a significant racial factor was shown in our data.

There are many sites in the intestinal tract involved in both groups (Table 2). Bowel obstruction was encountered in a few cases, but in many cases no cause could be found. There were no gastric perforations without pneumoperitoneum.

Many of the patients had congenital anomalies. The gastrointestinal anomalies included congenital bands, esophageal, biliary, duodenal and jeju-

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TABLE 1.—*Clinical Data on 25 Infants with Intestinal Perforation*

	<i>Pneumo-peritoneum</i>	<i>No Pneumo-peritoneum</i>
NUMBER OF CASES .....	16	9
AGE		
Under 1 Week .....	9	3
1 Week to 1 Month .....	2	2
Over 1 Month .....	5	4
Range .....	1 Day to 12 Weeks	2 Days to 6 Months
SEX		
Male .....	10	4
Female .....	6	5
RACE		
Caucasian .....	7	8
Non-Caucasian .....	9	1

nal atresia, malrotation, omphalocele, mesenteric defect with internal hernia, situs inversus of liver and stomach and megacolon. The cardiovascular anomalies were patent ductus arteriosus, atrial and ventricular septal defect and transposition of great vessels. There was one case of multiple epiphyseal dysplasia, congenita (stippled epiphyses).

The incidence of prematurity and obstetrical complications also was fairly high. Premature rupture of membranes, intrauterine fetal distress, cesarean section in a diabetic mother and complicated breech delivery were the obstetrical problems, aside from premature delivery. Nine of the 25 patients (36 per cent) were premature infants.

In the iatrogenic category, there was one rectal perforation by a thermometer. There are only five other such reported cases in this age group.<sup>2,4,7,14,17</sup> In four of the cases of gastric perforation, there was a questionable relationship between perforation and nasogastric intubation. The shape and large size of the gastric defects were such as to make one think of traumatic laceration, although this could not be proved. There are three published cases in which gastric perforation was attributed to intubation.<sup>3,7,11</sup>

The mortality in the present series was high—94 per cent in the group with pneumoperitoneum, 78 per cent in the group without and 88 per cent

overall. The only survivors were patients in whom surgical exploration was done. These figures are not unusual. Nice and Mouton<sup>9</sup> reported a series of 16 perforations in this age bracket with a 75 per cent mortality. Freeark and coworkers<sup>4</sup> reported 87 per cent mortality in 15 cases, and Tucker and Izant<sup>16</sup> a 50 per cent mortality in 26 cases.

It has been our experience that diagnosis of the site of perforation clinically or radiographically from plain films is almost impossible. The use of contrast media for gastrointestinal examination in suspected perforation is not productive of much useful information, delays operation, and may be harmful. Two of our cases with colon perforation had free spill of barium into the peritoneal cavity. While we may hope that better obstetrical and nursing care, prevention of prematurity and awareness of iatrogenic complications may reduce the factors predisposing to perforation, the best chance for cure is early diagnosis and prompt surgical exploration. The radiologist can perform a vital service in this regard.

The roentgen signs of perforation are pneumoperitoneum, peritoneal fluid and bowel distention. The features in radiographic diagnosis of pneumoperitoneum have been well described.<sup>6,8,12,13</sup> Some cases are easily diagnosed, while others are diffi-

TABLE 2.—*Site and Type of Intestinal Perforation in 25 Cases*

<i>Site of Perforation</i>	<i>Nature of Lesion</i>	
	<i>Pneumo-peritoneum (16)</i>	<i>No Pneumo-peritoneum (9)</i>
Stomach & Duodenum .....	Idiopathic gastric (3) Gastric ulcer (2) Duodenal ulcer (1)	Duodenal ulcer (5)
Jejunum & Ileum .....	Postoperative leak, ileal (3) Mechanical obstruction, ileum (3) Idiopathic ileal (1)	Jejunal ulcer (1) Mechanical obstruction, ileum (1) Meckel's diverticulitis (1)
Colon .....	Idiopathic transverse (1) Traumatic rectal (1)	Transverse, [Hirschsprung's] (1)
Cecum .....	Necrotizing colitis (1)	





Figure 1.—(Case 1) Supine film with pneumoperitoneum, seen as "football sign." The patient had necrotizing colitis of cecum with perforation.

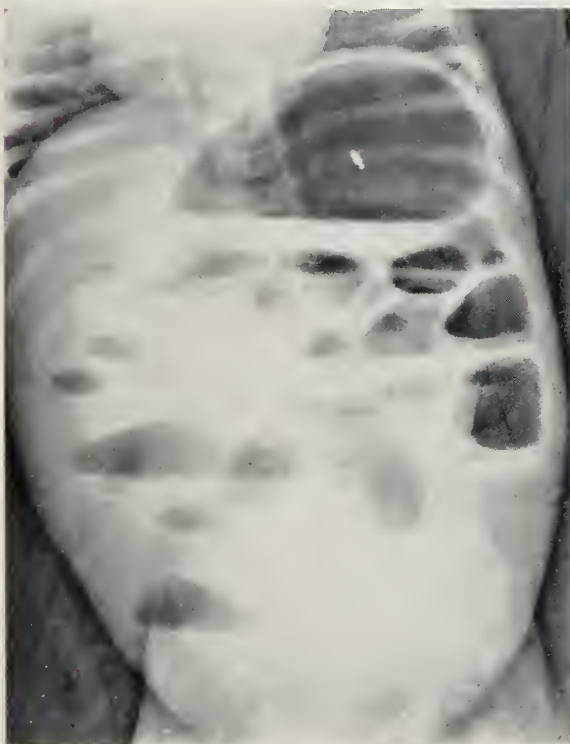


Figure 2.—(Case 2) Air in lesser peritoneal sac; peritoneal fluid; adynamic ileus. The patient had a perforated duodenal ulcer.

cult. Chances of detecting small amounts of free air are improved by taking two views of the abdomen, a supine and either an upright or lateral decubitus film. We shall present several illustrative cases from our series.

## Reports of Cases

**CASE 1.** A premature boy became ill at two days of age. Pregnancy had been complicated by rupture of the membranes one month before delivery. The baby appeared healthy at birth, but on the second day abdominal distention developed. However, the baby continued to pass meconium. A supine radiograph of the abdomen taken on the second day of life (Figure 1) showed gas in the stomach and some slightly distended gas-filled small bowel loops. There was a faint central oval radiolucency, and the falciform ligament was outlined. This is an example of the "football" sign, the oval radiolucency representing the ball, and the falciform ligament the lacing of the ball. Small amounts of air on a supine film collect under the anterior abdominal wall and over the liver, and can be subtle enough to be overlooked, unless one is specifically looking for it. At operation peritonitis and a cecal perforation due to necrotizing colitis were observed. There was also a defect in the mesentery with a closed loop ileal obstruction secondary to an internal hernia. The baby died one day after operation with Gram-negative septicemia. Autopsy was refused.

**CASE 2.** A two-month-old girl was admitted with a one-week history of diarrhea and dehydration. Stool cultures grew normal flora. Three days after admission abdominal distention was noted. On the tenth hospital day "coffee ground" emesis occurred, and abdominal roentgenograms were obtained. On the supine film, gas-distended intestinal loops were seen. Air-fluid levels in them were shown on the upright film (Figure 2). The hazy density to the abdominal contents and separation of intestinal loops suggested peritoneal fluid. Two large gas shadows were present in the left upper quadrant, one of them the gas-filled stomach, the other gas in the lesser peritoneal sac. This manifestation of pneumoperitoneum was not recognized at the time the films were taken. The patient died one day later. At autopsy, a duodenal ulcer with posterior perforation and peritonitis was found.

**CASE 3.** The patient was a three-week-old girl who had been born prematurely, by breech delivery, to an 11-year-old mother who had been impregnated by her father. The baby had short humeri, flexion contractures of the hips and knees, cataracts and heart murmurs. Skeletal roentgenograms showed multiple epiphyseal dysplasia (stip-

pled epiphyses). At three weeks of age, the infant became ill, with vomiting, constipation and abdominal distention. Abdominal films at this time showed free air. This was seen on the supine film as visualization of both walls of bowel loops, and more obviously on the upright film under the left hemidiaphragm. There were also distended loops of bowel with air fluid levels. At operation a perforation of the right transverse colon with peritonitis was found, as well as incomplete malrotation with a high cecum. The perforation was closed, but the baby died a day later with Gram-negative septicemia. At autopsy, no abnormalities in colon musculature, ganglion cells or blood supply were observed, and there was no evidence of bowel obstruction. Other findings were pulmonary stenosis, ventricular septal defect and stippled epiphyses.

CASE 4. A girl baby, premature, who was being gavage-fed had jaundice at two days of age and passed foul meconium and yellow stools. At five days, lethargy, irritability, anorexia and abdominal distention were noted. There was no emesis or constipation. Abdominal films were obtained at this time (Figure 3). The supine film showed the "football" sign and separation of gas filled loops indicating peritoneal fluid. The decubitus view showed a more obvious accumulation of air between the liver and costal margin. The baby died before operation could be done. At autopsy, a  $1.5 \times .8$  cm diamond-shaped laceration of the mucosa of the posterior wall of the stomach, with a 5 mm perforation through the serosa, was noted. The pathologists were uncertain whether the cause was ulcer, mural defect or traumatic laceration, but at last agreed on gastric ulcer.

CASE 5. The patient was a boy born at term, after premature rupture of membranes, to a mother with a positive reaction to a blood test for syphilis. Cyanosis and abdominal distention were noted on the first day of life, and were treated with oxygen and the placement of nasogastric and rectal tubes. The stools were normal. Subsequently, the baby vomited a green substance and passed blood-tinged stools. A supine abdominal radiograph at seven days of age revealed considerable free air, with a "football" sign and outlining of lateral peritoneal walls. At operation the same day, a 2 cm tear along the greater curvature of the stomach was found, as well as some thin duodenal bands and the presence of peritonitis. The bands were



Figure 3.—(Case 4) Decubitus view, with free air between liver and costal margin, and outlining outer wall of intestinal loops. Perforated gastric ulcer.

freed and the perforation was closed. The patient died in the postoperative period. Autopsy revealed hemorrhage and ulceration in the area of the repaired laceration. The final pathologic diagnosis was spontaneous (idiopathic?) perforation of the stomach.

CASE 6. The patient, a premature boy, had passed no meconium by 24 hours, and abdominal distention and regurgitation were noted on the second day of life. An upright roentgenogram of the abdomen revealed air under the diaphragm, gas-distended intestinal loops and a suggestion of peritoneal fluid. At operation volvulus of the terminal ileum with a gangrenous perforation, but no malrotation, were noted. The patient died in the postoperative period and autopsy was refused.

CASE 7. Abdominal distention, vomiting and anorexia developed in a five-day-old girl one day before admission. She was treated with nasogastric intubation. Abdominal radiographs on admission showed a large collection of free air over the





Figure 4.—(Case 8) Large pneumoperitoneum with air along the lateral peritoneal walls and over the liver. Spontaneous perforation of stomach.



Figure 5.—(Case 10) Massive pneumoperitoneum. Note air under the diaphragm, in the scrotum, outlining falciform ligament, lateral peritoneal walls, and outer walls of bowel loops. Adynamic ileus. Traumatic perforation of rectum.

right hemi-abdomen and liver on the supine view, and under the diaphragm on the upright film. At operation a 3 cm tear in the greater curvature of the stomach was seen. This was repaired, and the child recovered. Biopsy was not obtained. Final diagnosis was spontaneous (idiopathic?) perforation of the stomach.

CASE 8. A boy, born at term after intrauterine fetal distress, had been in respiratory trouble since birth. He required a tracheal catheter and oxygen. Meconium was passed. Emesis occurred on the first day, and abdominal distention on the third. Nasogastric intubation partially relieved the distention. Abdominal radiographs on the third day (Figure 4) revealed a large amount of free air over the liver, under the diaphragm and outlining the lateral peritoneal walls. At operation, peritonitis and a 5 cm tear along the lesser curvature of the stomach were noted. The perforation was closed. The patient died postoperatively and autopsy was refused. There was no biopsy of the stomach. The final diagnosis was spontaneous (idiopathic?) perforation of the stomach.

CASE 9. A girl, born at term, was admitted to hospital at one month of age with jaundice progressive since birth. Physical findings were icterus and enlargement of the left lobe of the liver. Mild hemolytic anemia due to ABO incompatibility was present. The clinical course was complicated by sepsis, but after prolonged medical treatment the infant's physical condition improved. The jaundice persisted, however. Laparotomy was done at two months of age, and atresia of the common bile duct, with biliary cirrhosis, was observed. Cholecoduodenostomy was performed. Also noted was situs inversus of the liver and stomach. The postoperative course was complicated by sepsis, but the infant appeared to be making a reasonable recovery. A month after laparotomy, abdominal distention and vomiting developed. Roentgenograms of the abdomen at this time revealed free air in the right upper quadrant and under the diaphragm, as well as gas-distended intestinal loops with air-fluid levels on the upright film, suggesting bowel obstruction. Death occurred suddenly, before operation could be done. At postmortem examination a band obstruction of the terminal ileum, with perforation and peritonitis, were observed.

CASE 10. A boy, born prematurely, was trans-

ferred to the Los Angeles County General Hospital from a suburban hospital at three days of age. On admission, physical findings were cyanosis, tachypnea, retractions and abdominal distention. The rectal temperature was 95°F. Meconium was passed. A supine radiograph on admission (Figure 5) showed massive pneumoperitoneum, with air under the diaphragm, in the scrotum, over the liver outlining the falciform ligament, and outlining the lateral peritoneal walls and outer walls of bowel loops. A pattern of ileus was also present. At operation, a perforated opening the size of a thermometer bulb was found in the anterior rectal wall just above the peritoneal reflection. Peritonitis was present. The patient died during operation. Autopsy revealed no defects in blood supply, no ganglion cells or smooth muscle of bowel wall and no evidence of malrotation or bowel obstruction.

CASE 11. The patient, a girl, was delivered at term, of a diabetic mother, by cesarean section. She had had respiratory distress with cyanosis from birth. Roentgenogram obtained on the third day of life revealed pneumonitis and an intestinal pattern compatible with mild, adynamic ileus. There was no evidence of free intraperitoneal fluid or air. Subsequently, abdominal distention developed, and the infant died on the fifth day. Repeat films were not obtained before death. Postmortem examination revealed pneumonitis, perforated duodenal ulcer, peritonitis and Gram-negative septicemia. It is possible that had films been obtained after abdominal distention developed, they would have revealed free air.

## Conclusion

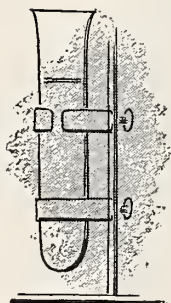
Early radiographic examination of the abdomen appears to be the most important step in improving the mortality rate associated with intestinal

perforation in early infancy. Awareness of the roentgen features, predisposing factors and non-specific clinical manifestations may lead to earlier diagnosis and treatment.

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# LUNG CANCER

## Improved Cytologic Detection by Inducing Production of Sputum

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■ *The principle of producing bronchial lavage by deposition of large amounts of heated aerosol has resulted in a significantly greater yield of positive cytologic diagnosis of bronchogenic carcinoma than with repeated "volunteer" specimens of sputum. Positive pressure plus bronchodilators augments greater sputum volume.*

*Using this technique, cases in which results of bronchoscopy and aspiration biopsy were negative for malignant change, were diagnosed cytologically.*

*Application of this technique can sometimes detect early lung carcinoma before roentgenographic changes are detectable. Positive tests in clinically far advanced disease may prevent unnecessary surgical intervention.*

*The simplicity of the technique, the freedom from adverse reactions, and its wide acceptance by the subjects tested, make it valuable in the diagnosis of lung cancer.*

BRONCHIAL LAVAGE is produced by deposition of large amounts of heated aerosol together with the condensation of water vapor on the relatively colder surfaces of the respiratory passageways. This is achieved by inhaling an aerosol mist at approximately 125°F, from a volume-producing nebulizer which liquefies retained secretions and aids in their expectoration.<sup>2</sup>

Factors which determine the degree of retention of an aerosol and the sites of deposition within the respiratory tract are: The particle size and density, vapor pressure, temperature, the hygroscopic properties of the aerosol and the rate and depth of respirations.

Ninety-seven per cent of solid particles of 1 micron or less are deposited within the lung. Particles of 3 micra in radius are taken out completely by the trachea, the bronchi and the bronchioles. Wilson and La Mer<sup>10</sup> reported maximal retention of approximately 50 per cent in the alveoli and bronchioles with particles of 1 micron in radius.<sup>10</sup>

The stability of a water droplet 0.5 micron in radius under ordinary conditions of humidity is only a fraction of a second, due to its high evaporation rate. Furthermore, rapid absorption of isotonic aerosols takes place within the tracheobronchial tree.

Studies by Abramson<sup>1</sup> indicated that droplet evaporation is decreased with aerosols in a gly-

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TABLE 1.—*Comparison of Cytologic Diagnosis of Spontaneous and Induced Sputum in Patients with Suspected Pulmonary Malignant Disease*<sup>2</sup>

	No. of Cases	Positive for Malignant Cells	Suspicious Abnormal Cells	Negative for Malignant Cells
Spontaneous sputum*	14	2	2	6
Induced sputum	14	9	5	

\*Four specimens unsatisfactory for cytologic study.

cerin solution, the reduction in vapor pressure serving to stabilize the aerosol mist. Decreased deposition of a mist occurs if the aerosol is heated; also, heating decreases irritation to the respiratory tract and reduces viscosity.

Impingement of an adequate number of hypertonic saline droplets upon the bronchial mucosa will induce transudation by osmosis; such bronchial transudate washes exfoliated cells into the material subsequently expectorated.<sup>3</sup>

The striking differences in the results obtained with induced sputum as compared with those from spontaneous specimens may perhaps be explained by the following possibilities: (1) Poor preservation of the cells in spontaneous sputum by reason of varying periods of retention within the tracheo-bronchial airway; and, (2) a mixture of saliva and postpharyngeal secretions, producing a "dilution" effect on the bronchial secretions.<sup>2</sup>

Barach and coworkers<sup>2</sup> compared methods of spontaneous and induced sputum technique in the same 14 patients suspected of pulmonary malignant disease. A significantly higher yield of malignant cells was obtained with the induced sputum technique (Table 1).

## Material and Method

Inhalation of 15 per cent sodium chloride combined with 20 per cent propylene glycol preheated to 160°F is used. The aerosol at the end of the mouthpiece is approximately 110°F to 120°F. The inhalation period is approximately 30 minutes.

At the end of that time a specimen is collected and the patient is handed a sterile specimen flask, containing 95 per cent ethyl alcohol fixative, and is instructed to spit into it all sputum during the ensuing 24 hours.

The use of intermittent positive pressure breathing accomplishes better distribution of air (and aerosol) throughout the lung parenchyma.<sup>7</sup>

In the present series a 1:200 Isuprel solution was introduced into the circuit to enhance bronchial lavage.

Either oxygen or compressed air\* can be used for gas flow.

## Reports of Cases

CASE 1. An 84-year-old farmer, a non-smoker, had been in good health, except for duodenal ulcer treated in 1959, until an episode of influenza in January of 1963. Cough and shortness of breath developed and an ejection systolic cardiac murmur was noted. The patient was in congestive heart failure and was digitalized. He improved for a few weeks. However, fluid formed in the right pleural space and he subsequently had weight loss and increasing dyspnea. On 17 January 1963, thoracentesis revealed pleural fluid, and a cell button highly suspicious of malignant cells. An x-ray film of the chest subsequent to the thoracentesis revealed no definite mass in the right lung but did show a prominence of the right hilus. Bronchoscopy in January of 1963 with bronchial biopsy revealed no tumor. The histologic diagnosis was chronic bronchitis. On 4 February 1963, an x-ray film showed atelectasis of the right middle lobe with associated soft tissue mass in the lower right hilum and right pleural effusion. On 17 February, a 24-hour voluntary sputum specimen, not induced, was negative for malignant cells. Bronchial washings at the time of bronchoscopy were negative for malignant cells.

On 25 February sputum induction with heated aerosol inhalation revealed atypical suspicious cells present, probably malignant (Class III or IV). A review of previous cytologic studies on pleural fluid showed similar cells present. In consultation a thoracic surgeon concurred with the diagnosis of inoperable lung tumor.

CASE 2. The patient, a 77-year-old white man, a retired citrus orchardist, had smoked 20 cigarettes a day for 40 years. He had been losing weight, had been chronically fatigued and had had shortness of breath on exertion for several months. He complained of chronic cough which he had had for two years, and in recent months he had had pain in the left side of the chest. X-ray

\*Mistogen, Temp-trol model CY-2.



studies of the chest demonstrated atelectasis of the left upper lobe and pleural effusion.

Bronchoscopy showed a tumor obstructing the left upper lobe bronchus. This mass was visualized directly by use of an angled mirror.

Pleural fluid submitted for cell button and cytologic studies was reported as negative for malignant cells by the pathologist. The scalene lymph nodes resected from the left were also reported negative. Bronchial washings contained "insufficient cells" for adequate study. A study of a 24-hour specimen of sputum, non-induced, collected by the patient was reported as negative for malignant cells.

The clinical diagnosis was bronchogenic carcinoma, left upper lobe, with atelectasis of the left upper lobe and pleural effusion on the left.

A 24-hour specimen of induced sputum was reported by the pathologist as positive for malignant cells, Class V, squamous.

The tumor was considered inoperable.

**CASE 3.** The patient, a 54-year-old food handler, who had smoked about 20 cigarettes a day for many years, complained of thoracic discomfort and pain in the back for two months. An x-ray film of the chest showed a cavitating lesion of the left upper lung reported as "most likely carcinoma." This was confirmed by pneumonectomy.

An induced sputum specimen and cell button studies were positive for malignant cells, Class V.

Within two months after pneumonectomy the patient was in a terminal stage of disease with widespread node and bony metastasis.

Patients with cavitory lesions are excellent candidates for screening for malignant disease by the heated aerosolized induced sputum technique.

**CASE 4.** A 68-year-old man, a painter, complained of a dull ache in the left anterior chest and later cough and hemoptysis. A physician had administered antibiotics with no appreciable effect. The thorax was symmetrical, breath sounds were normal and there were no rales. The heart was of normal size with a regular rhythm and no murmurs. An x-ray film of the chest revealed infiltration of the left lung field and the region of the lingular segment of the upper lobe. This was thought to be due to lobar pneumonia. Results of bronchoscopy were negative and a bronchial biopsy revealed no pathologic change in bronchial

mucosa. Bronchial washings were reported as negative for disease. On biopsy of a scalene node taken from the left side, the morphologic structure was that of a rather anaplastic carcinoma compatible with carcinoma of the lung or of the pancreas.

Examination of sputum induced by heated aerosol inhalation revealed highly atypical cells that, on cell button examination, were suspicious of carcinoma.

Carcinoma of the lung with supraclavicular node metastasis and probably metastasis to the lumbar spine was diagnosed.

Subsequent palliative treatment with 5 fluorouracil, 1 gram daily for six days, followed by local x-ray therapy to the lumbar spine area was given. The condition of the patient deteriorated rapidly.

In this case, earlier resort to a screening test by induced sputum could have prevented an unnecessary scalene node biopsy. This case serves as an example of the usefulness of detecting metastatic lung disease as well as primary lung carcinoma.

**CASE 5.** The patient, a 59-year-old salesman who had smoked 40 cigarettes a day for many years, had a "chest cold" with a dull aching in the chest above the left breast. Coughing was productive of a tannish exudate and occasional foul green sputum.

On physical examination, dullness to percussion was noted over the left upper lobe posteriorly and anteriorly.

An x-ray film of the chest showed left upper lobe opacification primarily in the area of the apical posterior segment. Bronchial compression or obstruction was considered probable.

Sputum induction with heated aerosol inhalation produced results as follows: First specimen, smears and cell button positive for Class V squamous cells. Second specimen (24 hours), smears positive for Class V squamous cells.

On bronchoscopic examination no tumor could be seen—only purulent sputum exuding from the left main stem bronchus. Scalene nodes were removed from both sides. On gross examination they appeared normal and the specimens were not submitted to the pathologist.

Thoracotomy was carried out a week after the induced sputum examination. On biopsy of the left upper lobe and a mediastinal node a diagnosis

TABLE 2.—Results of Sputum Examination for Cancer Cells in 77 Patients with Proved Lung Cancer<sup>5</sup>

Diagnosis	Total Patients	Total Positive	Routine Specimen	Patients with Cancer Cells in Sputum	
				Induced Specimen	
				Total Direct	Delayed Only
Bronchogenic carcinoma .....	59	33	9*	28	4
Metastatic cancer to the lung.....	18	9	2*	7	1

\*Induced specimen negative in one patient but positive in others.

was made of primary bronchogenic squamous cell type carcinoma, inoperable.

In this case, after the induced sputum specimens were positive for squamous cell carcinoma of the lung, subsequent bronchoscopy and scalene node procedures could have been avoided and exploratory thoracotomy carried out.

## Discussion

Papanicolaou<sup>8</sup> reported several instances in which the sputum smear supplied the first evidence of malignant neoplasm. In some cases malignant cells were seen in the sputum smears when results of bronchoscopy and aspiration biopsy were negative. In one case in which three successive aspiration biopsies were negative, the sputum smear was positive and revealed "several abnormal cells offering conclusive evidence of malignancy and slight metaplasia." Subsequent exploratory thoracotomy showed inoperable cancer of the lung.

Farber<sup>4</sup> discussed the clinical applications of cytologic diagnostic technique and said that it is of value to the thoracic surgeon in establishing a reliable preoperative morphologic diagnosis of lung cancer. A positive cytologic diagnosis may be made in many cases in which, the lesions being located in the periphery of the lung or upper lobe bronchi, bronchoscopic examinations are of limited value. Difficult diagnostic problems may be solved when a definite morphologic diagnosis of cancer is made by positive cytologic studies. In patients with coexistent pulmonary tuberculosis and bronchogenic carcinoma, cytologic studies may clarify confusing clinical symptoms.

Cytologic studies of sputum may be utilized as routine screening procedures on patients with minimal or no pulmonary symptoms.

In Farber's series of pathologically proven bronchogenic cancer, a positive cytologic diagnosis was made oftener and sooner than was diagnosis by morphologic studies. In 47 per cent of these cases cytologic examination was the first diagnostic procedure to establish a morphologic diagnosis.

Fontana and coworkers<sup>5</sup> used the induced spu-

tum technique in 201 cases in which cancer was suspected. Of the 77 patients subsequently proven to have lung cancer, 40 (52 per cent) had cancer cells in induced sputum specimens. Induced sputum specimens were positive for cancer cells in eight of 18 patients with proven metastatic cancer to the lung (Table 2).

Umiker and coworkers<sup>9</sup> used the heated aerosol technique after "volunteer" sputum had already been examined, and thereby increased the positive cytologic diagnosis of cancer of the respiratory tract from 68.8 per cent to 87.5 per cent in a group of 32 histologically proven cases. Then, on repeated induction, 96.9 per cent of the patients had positive or suspicious smears.

Since the procedure for inducing sputum is not a demanding one, patients readily accept it and usually have no objection to repeating it if additional studies seem advisable. As the criteria for establishing the diagnosis are well established, the number of false positive and false negative reports is kept to a minimum. Bronchial epithelial cells and alveolar phagocytes identify the source of the specimens.

Carcinoma of the lung can sometimes be discovered by cytological examination of sputum before roentgenographic changes are detectable.<sup>6</sup> The lesions in such instances are usually small, centrally located, epidermoid, bronchial carcinomas hidden by mediastinal or hilar shadows; or they may still be in situ or only superficially invasive.

Experience with this technique is still limited, but it would appear to have value for screening all adult patients with respiratory symptoms or signs and those in whom the risk of lung cancer is increased by age and heavy smoking or by previous oral or laryngeal carcinoma. The use of induced sputum for diagnosis may save the patient with advanced and inoperable lung cancer needless surgical procedures.

It is believed earlier diagnosis will be made when cytologic techniques are applied immediately after cancer is suspected and when this diagnostic



method is utilized on patients with equivocal lung lesions detected by routine roentgen surveys. Also, when patients with cough and sputum—whether cancer is suspected or not—are routinely studied by cytologic techniques.

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# The Long-Term Effectiveness of Methyldopa in Hypertension

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AND MORTON H. MAXWELL, M.D., *Los Angeles*

■ *A trial of methyldopa in hypertension was conducted in 60 patients for a mean time of 9.4 months. Initially, four different dosages of methyldopa were studied and blood pressure was significantly lowered in the supine and standing positions. Standing blood pressure was significantly reduced more than supine. An average of 5.2 visits passed before maintenance blood pressure was obtained. There was no significant evidence of deterioration during the duration of this study. Side effects were mild. Only two patients voluntarily requested discontinuance of this study. Tolerance to the drug occurred and approximately 50 per cent of the patients no longer had a significant blood pressure reduction to methyldopa alone by the end of the study. Methyldopa appears to be a significant addition to the drug therapy of hypertension.*

METHYLDOPA HAS BEEN found to be a useful drug in the short-term treatment of primary hypertension<sup>1,3,4,5,6</sup> and of hypertension due to renal disease. There have been few studies of the long-term effects of methyldopa in the treatment of hypertension.

The purpose of this report is to present data on the long-term follow up of a large group of patients with hypertension, both primary and secondary, in an attempt to assess the relative value of methyldopa as an antihypertensive drug.

## Methods

### Sixty patients in the Renal Hypertension Clinic

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of the University of California Health Center at Los Angeles were used in this study. No attempt was made to exclude patients whose hypertension was of renal origin. (Patients were included in the study as they presented themselves to the clinic for therapy.) For inclusion in the study, it was required that the diastolic blood pressure average 100 mm of mercury or greater during the control period while the patient was receiving placebo. No patient received hypotensive drugs during the control blood pressure readings. Any of the following conditions excluded patients from this study: (1) Unwillingness or inability to attend the clinic; (2) Myocardial infarction, cerebral vascular accident, uncontrollable concurrent severe disease, such as neoplasm; (5) Accelerated (malignant) hypertension.

All patients screened initially were accepted for



the trial. At the time of the initial admission, each patient was interviewed by one of the physicians participating in the study. An effort was made to explain the purpose of this study and the need for perfect attendance. A history form was completed and a physical examination was done. The work-up included a recording of the blood pressure in the right arm immediately upon lying down and five minutes after standing, using the cessation of sound as the time for recording the diastolic blood pressure. The optic fundi were graded on the basis of hypertensive changes. Each patient received an intensive work-up to determine the etiologic factor in his hypertension. Included in this work-up was a roentgenogram of the chest, an electrocardiogram, determination of serum creatinine and serum electrolytes, urinalysis, urine culture, intravenous pyelogram, phenosulfonphthalein excretion, phentolamine test and/or urinary catecholamine excretion, complete blood cell counts and, when indicated, individual kidney function studies and renal arteriography.

The 60 patients were randomly allocated to one of four treatment groups by the physicians participating in the trial. No attempt was made to have a double-blind procedure and a single-blind protocol was followed throughout the study. Twenty-eight patients received methyldopa, 250 mg three times a day and 500 mg at bedtime (Group 1); 13 patients received methyldopa, 250 mg four times a day (Group 2); 13 received methyldopa 250 mg every eight hours (Group 3), and six received methyldopa, 250 mg every 12 hours initially (Group 4). As the study progressed, however, dosages were changed and a diuretic (chlorothiazide) was added to the regimens of pa-

tients who showed signs of congestive failure or who needed more adequate control of blood pressure. No dietary restrictions, other than those which had been given to the patient before the beginning of this study, were imposed. No additional medications were given.

Analyses of variance were performed to determine if the four groups differed significantly during the control period with regard to age, supine and standing blood pressures, serum creatinine and hypertensive retinal vascular changes. Student's t-test for paired data was used for comparison of the control and post-treatment data within each group. In this study a P value (probability) of less than 0.05 was the criterion for statistical significance.

Maintenance blood pressure (post-treatment) was arbitrarily taken as that time in the patient's treatment period when his blood pressure seemed to remain relatively stable and well controlled with one particular dosage regimen of methyldopa.

## Results

Table 1 lists the control blood pressures for all groups combined, the control blood pressures (supine and standing) for each of the individual four groups, the average values for serum creatinine, funduscopic examinations, age, sex distribution and number of patients with left ventricular hypertrophy. Analyses of variance showed no difference between the groups (P greater than 0.05) for supine and standing systolic and diastolic blood pressures, age, serum creatinine and funduscopic grading. The incidence of left ventricular hypertrophy and sex distribution appeared approximately equivalent between the groups. All

TABLE 1.—Control Values for Groups

Group*	Mean Average Blood Pressure (mm of Mercury)	Mean Average Serum Creatinine (mg per 100 ml)	Mean Average Funduscopic Grade (Keith- Wagener)	Number of Patients with Left Ventricular Hypertrophy	Sex	Average Age in Years
I	Supine 191.2/114.1 Standing 179.6/113.0	1.96	1.8	24	M 33 F 27	51.6
II	Supine 192.4/116.3 Standing 182.6/116.0	1.6	1.8	8	M 15 F 13	50.0
III	Supine 178.2/109.4 Standing 168.2/105.7	1.4	1.5	6	M 7 F 6	53.1
IV	Supine 199.9/113.7 Standing 182.4/113.5	2.1	1.8	7	M 7 F 6	55.6
All	Supine 193.3/113.3 Standing 182.0/112.3	2.7	2.4	3	M 4 F 2	48.0

\*For description of groups, see text.

patients were Caucasian except for two Negro women (both in Group 3).

Of the total of 60 patients 33 were males and 27 females. It was determined that 11 patients had hypertension secondary to renal disease (four in Group 1, two in Group 2, two in Group 3 and three in Group 4). Forty-nine patients were considered to have primary hypertension. The age range was 17 to 76 years, with a mean of 51.6 years. Serum creatinine had a mean of 1.96 mg per 100 ml with a range of 0.5 to 15.0 mg per 100 ml. A total of 24 patients showed left ventricular hypertrophy by electrocardiogram and chest roentgenogram criteria. Fundoscopic examination revealed a range of grade 1 to 3 with a mean of 1.8 on a grading system of 1 to 4 (Keith Wagener). Previous therapy in this group of patients was as follows: No therapy for 34 patients; chlorothiazide, 10 patients; reserpine, two patients; guanethidine, three patients; various experimental medications, three patients; hydralazine, three patients; meprobamate, three patients; phenobarbital, one patient.

Mean duration of treatment with methyldopa was 9.4 months with a range of one to 23 months. During this time, patients were seen a mean number of 13.0 times with a range of two to 35 visits. In addition, patients were seen a mean of 2.2 visits on control (placebo) medications. Patients were continued on placebo medication until it had been determined that their blood pressure was stable. At this time they were begun on active drug therapy. A mean of 5.2 visits was necessary to obtain stability and good control of blood pressure (maintenance blood pressure); the range was one to 14 visits.

Table 2 shows the blood pressure on control and active medication with the difference in supine and standing systolic and diastolic pressures. Each of the four groups showed a statistically significant difference in supine and standing systolic and diastolic blood pressures between control and active therapy ( $P$  less than 0.05). Analyses of variance did not show any statistically significant differences between the results of the four groups in response of blood pressure to methyldopa in any position, either systolic or diastolic. That is, the blood pressure changes were comparable in all four groups.

In all groups, except Group 2, standing blood pressure was lowered more than supine blood

TABLE 2.—Blood Pressure Changes (mean average, mm of mercury) Between Treatment with Placebo and Methyldopa

Group*		With Placebo	With Methyldopa	Difference
I	Supine	192.4/116.3	160.7/99.2	31.7/17.1
	Standing	182.6/116.0	140.8/91.6	41.8/24.4
II	Supine	178.2/109.4	149.3/93.8	28.9/15.6
	Standing	168.2/105.7	140.6/89.8	27.6/15.9
III	Supine	199.9/113.7	173.2/101.2	26.7/12.5
	Standing	182.4/113.5	144.5/94.5	37.9/19.0
IV	Supine	193.3/113.3	156.5/97.3	36.8/16.0
	Standing	182.0/112.3	138.5/86.0	43.5/26.3

\*For description of groups, see text.

pressure ( $P$  less than 0.05 in Groups 1, 3 and 4); in Group 2 there was no significant difference. Qualitatively speaking, the control of blood pressure with methyldopa was divided into three categories as follows: Poor control was defined as mean blood pressure (mean blood pressure is diastolic blood pressure plus one-third of the pulse pressure) reduction by less than 10 per cent; fair control was arbitrarily defined as a 10 to 20 per cent reduction in the mean blood pressure, and good control was defined as greater than 20 per cent reduction or normotension. Using these criteria, it can be seen from Table 3 that 37 of 60 patients had good control of blood pressure, 12 of 60 had fair control and only 11 of 60 had poor control in the standing position. However, in the supine position only 22 of 60 patients had good control, 21 of 60 had fair control and 17 of 60 had poor control. There does not appear to be any obvious difference in the qualitative degree of control of blood pressure between the four groups. All groups seem to show the same tendency as noted for the total pooling of patients in all groups.

Although most patients seemed to remain at their maintenance blood pressure reductions for a reasonable length of time, all patients required periodic adjustment in methyldopa dosage to maintain this significant blood pressure response. Slowly dosages were increased until it became obvious that some patients no longer responded optimally. Twenty-nine of the 60 patients were receiving 1.250 gm per day of methyldopa, 15 of the 60 were receiving 2.0 gm per day and the remaining 16 patients fell between these two extremes. Several patients had methyldopa dosage raised to 5 gm per day in an attempt to further lower blood pressure, but this had no increased hypotensive effect over 2.0 gm per day. By the end of the study, 32 of the patients no longer had



TABLE 3.—*Qualitative Degree of Blood Pressure Control*

Group	Supine			Standing		
	Poor	Fair	Good	Poor	Fair	Good
I (28 patients)	6	13	9	3	7	18
II (13 patients)	4	2	7	3	2	8
III (13 patients)	5	4	4	5	2	6
IV ( 6 patients)	2	2	2	0	1	5
All (60 patients)	17	21	22	11	12	37

\*For description of groups, see text.

a significant blood pressure reduction from methyl-dopa alone and other medications were required to control their blood pressure. Seven patients received chlorothiazide and 25 patients were dropped from the study and the use of other drugs was begun. This development of tolerance appeared to be gradual and not sudden.

Only minor toxic effects of methyl-dopa were noted in this study. The total number of side effects noted was large, but usually each patient had more than one symptom. Thirty of the 60 patients noted drowsiness, which tended to disappear after a few days on a particular dose. However, when the dosage was adjusted upward the drowsiness usually recurred for a few more days. Two patients complained spontaneously of being depressed, but this was not considered to be serious by the physicians. Five patients admitted to diarrhea and none complained of constipation. Two patients complained of dry mouth, four of blurred vision, four of nausea and three of decreased libido.

At no time during the study were changes noted in the complete blood cell count. There were no changes in bilirubin and there were only minor and transient creatinine changes—four patients had a decrease in serum creatinine. Three patients had rises in serum glutamic oxalacetic transaminase. In none of these patients were these rises permanent, but rather the elevations occurred sporadically during the routine determination of this test. There were no signs or symptoms of liver toxicity by any other measurement. In one patient myocardial infarction developed during treatment. He was normotensive at the time of infarction. This was not considered to be drug-related. Only mild and spontaneous changes were noted, both of improvement and deterioration, in retinal findings. Two patients wished to be dropped from the study because of side effects; one of these patients complained of diarrhea and the other of drowsiness. The diarrhea occurred after five months on methyl-dopa and the drowsiness after one month. The

data on these two patients were included in the study.

## Discussion

The main objective of this study was to determine the long-term effects of methyl-dopa in the treatment of hypertension. Our work agrees with that of others who found that methyl-dopa will significantly lower blood pressure in hypertensive patients.

This drug brings about a more significant drop in standing blood pressure than in supine. This agrees with the findings of Wilson<sup>1</sup> and coworkers.

Many clinicians feel that methyl-dopa is a useful hypotensive agent only for reasonably short-term therapy—less than six months. They feel the tolerance to this agent occurs quickly and permanently. Our data indicate that approximately half of patients will gradually develop tolerance to the hypotensive action of methyl-dopa within a mean time of 9.4 months. It became obvious, near the end of the study, that even those patients still sensitive to methyl-dopa, no longer responded as well with blood pressure lowering as they had done at the beginning of the study and required upward revision of dosage.

With the exception of one patient, none of the patients in the series had deterioration of condition in any way that could be attributed to his hypertension during this study. This one patient developed a myocardial infarction as noted previously. In fact, serum creatinine although not significantly changed, showed a minor decrease and retinal vascular tortuosity showed no change during the study. Only two patients felt they could not tolerate the medication because of adverse effects. In our experience, this is less than we might have expected from other hypotensive agents. Although the sedation was bothersome to some patients, the majority of patients did not seem to complain.

Although standing blood pressure was lowered

more than supine blood pressure, the hypotensive action of methyldopa appears, at these doses, to be reasonably strong. Other studies indicated that methyldopa, given alone, produces a disappointing reduction in blood pressure in most patients.<sup>4</sup> Methyldopa was not as easy to use as we had thought before our study. A mean of 5.2 visits was necessary before reasonable reductions in blood pressure were obtained. This points up the need for frequent visits and adjustment in dosage of methyldopa before stable blood pressure reduction is obtained. Our data also indicate that there is a wide dosage range for maintenance blood pressure reduction—500 to 1,250 mg per day. Clinicians have occasionally noted striking and profound hypotensive responses to small doses of methyldopa, even in patients with accelerated hypertension. Thus, the six patients who had significant blood pressure lowering from methyldopa in a dosage of 250 mg every 12 hours, might be comparable to the three patients of the 30 who received methyldopa in a study by Wilson and coworkers<sup>6</sup> who developed hypotension (systolic blood pressure less than 100 mm of mercury). However, near the end of the study, the minimum dosage of methyldopa which a patient required was 1,250 gm per day and a fourth of the patients required 2.0 gm per day to maintain a significant blood pressure reduction. In addition, seven of the 60 patients needed diuretic therapy in addition to methyldopa. Probably blood pressure reduction would have

been more significant had all patients been placed on thiazide therapy, since Wilson and coworkers<sup>6</sup> showed that the combination of methyldopa and a thiazide was more potent than methyldopa alone.

Our results are in close agreement with those of other workers regarding qualitative control of blood pressure.<sup>2</sup> Thirty-seven of our 60 patients had good control in the standing position and 22 of the 60 had good control in the supine position. Although this is somewhat disappointing, as far as supine blood pressure is concerned, the relative lack of severe adverse reactions combined with a reasonable incidence of good blood pressure lowering makes methyldopa a significant addition to the physician's armamentarium.

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# Quick Tracheotomy

## Incision at an Easily Identifiable, Relatively Safe Site

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From the time they begin their medical education, physicians have the importance of an adequate airway impressed upon them. Without one, all other procedures to save an injured patient are futile. But knowing the importance of quickly establishing an airway may be a long way from actually doing what is necessary in an emergency, as the following two case reports illustrate.

### Reports of Cases

Case 1. A patient was admitted to a hospital with multiple fractures of the mandible. He appeared to be in a stable condition but the house officer reported that when he was placed on his back on an x-ray table, obstruction of the airway occurred. Elevating the shattered mandible did not relieve the obstruction. Intubation was impossible because the patient had a "bull" neck, and the tongue was swollen. A tracheotome was then inserted but missed the trachea and lacerated the external jugular vein. On another attempt at insertion, the thyroid isthmus was lacerated, the tracheotome dissecting laterally into the soft tissues of the neck and causing diffuse bleeding. A third attempt was also unsuccessful because the neck of the patient was so thick and swollen that the trachea could not be accurately palpated. The house officer then attempted a "classic" tracheotomy under impossible circumstances. The patient died.

Case 2. A patient was admitted to the hospital with diagnosis of a fracture of the larynx that had

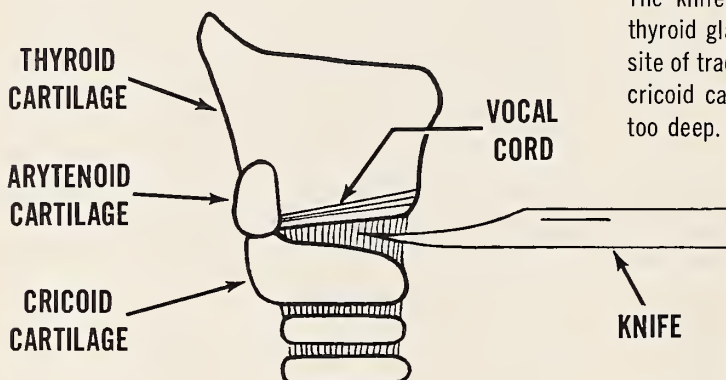
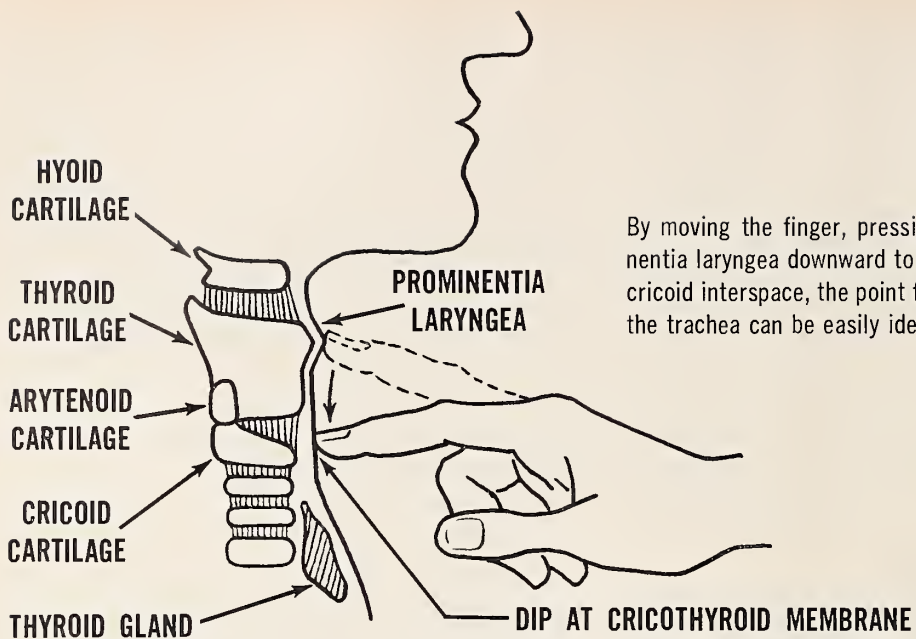
occurred in an automobile accident. He was hoarse but had a "relatively" patent airway. Later that evening the patient had a violent coughing spell and air was forced into the neck through the torn laryngeal mucosa, causing obstruction by compression of what little airway remained. An anesthesiologist happened by, but the laryngeal structure had been so distorted in the automobile collision that he could not identify any landmarks nor find the glottis on direct laryngoscopy. He started to carry out tracheotomy but massive emphysema and the traumatic distortion in the area made it impossible for him to find the trachea and make an opening in it.

Tracheotomy would have saved the patients in both cases, but the optimal conditions and the assistance needed for successfully carrying out the procedure usually are not to be had in situations of emergency.

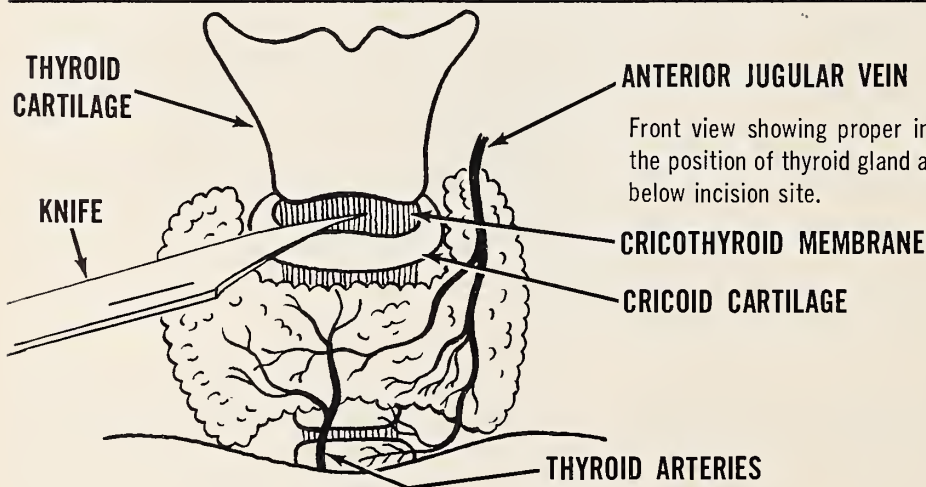
It is the purpose of this paper to discuss a simple and reliable method of establishing a temporary airway until an orderly tracheotomy can be carried out. The procedure is called a coniotomy (cricothyrotomy) or cutting of the cricothyroid membrane. It requires no special instruments and little knowledge of anatomy, and it can be done anywhere under almost any conditions.

### Anatomy

The cricothyroid membrane lies near the surface and can easily be palpated no matter how fat the neck may be. In contrast, the trachea lies deeper and even in slender persons it is not easily



The knife enters a relatively safe area well above the thyroid gland and the blood vessels that make the usual site of tracheotomy hazardous. The posterior aspect of the cricoid cartilage prevents thrusting the tip of the knife too deep.





felt. There are no vital structures superficial to the cricothyroid membrane whereas the trachea lies beneath numerous vessels and the very vascular thyroid isthmus.

## Method

The only instrument necessary for cricothyrotomy is a knife. A scalpel is preferable but not always readily available. A small pen knife of the type found on a key ring is adequate and is usually at hand. A detailed knowledge of anatomy is not needed, for there is an easy landmark, the laryngeal prominence (Adam's apple), that will lead to the cricothyroid membrane. It is necessary only to move a finger downward from the prominence, along the contour of the thyroid cartilage, to an indentation which identifies the cricothyroid membrane. With the larynx supported between two fingers of one hand, the point of the knife is pressed three quarters of an inch into the membrane. As the space between the cartilages is at

right angles to the plane of the neck, the knife must be positioned accordingly and the incision enlarged to 1 to 2 inches long. The larynx can even be transected at that point if necessary. As there are no vital structures in the immediate vicinity, even if the knife goes too deep it will stop harmlessly against the posterior aspect of the cricoid cartilage, missing the esophagus, which is below, and the vocal cords, which are above. The barrel or the cap of a pen, a finger or almost anything except a sharp object that could injure the cricoid cartilage can be used to keep the wound open until a definitive tracheotomy can be done. If need be, mouth breathing over the wound can be carried out.

The advantages of this method over the use of tracheotomes and a hastily performed "classic" tracheotomy are obvious. A cricothyrotomy can be done anywhere, without bright light, special instruments or assistance.

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# William M. Gwin, M.D.

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MEN OF MEDICINE have contributed much to California, not only in the field of medicine but in other areas of endeavor. William McKendree Gwin, M.D. was such a man. He was California's premier statesman, one of its first two United States Senators and, next to General John C. Fremont, deserving of more credit than any other man for making California a part of the Union.

The controversy that plagued him and which finally led to his political demise was in part based on his Southern birth and background. In a period of violent emotional turmoil and hatred which preceded the Civil War, everyone's actions were suspect. Undoubtedly, some of Dr. Gwin's activities were motivated by his Southern inheritance; nevertheless, his unceasing devotion to California especially during his tenure in office as U.S. Senator in Washington, cannot be denied.

William Gwin was born in Sumner County, Tennessee, 9 October 1805. His father was a Methodist frontier preacher and a "crack Indian fighter." William studied law but through a distrust of his own ability to become an effective public speaker decided not to enter the legal profession. He turned to the study of medicine and enrolled in the Medical Department of Transylvania University, Lexington, Kentucky, obtaining his M.D. degree with special honors in 1828. The school is now a part of the University of Kentucky. Another future Californian, Dr. H. H. Toland, founder of the Toland College of Medicine in San Francisco, was a member of the same class. Dr. Gwin's thesis of 23 closely written pages is preserved today in the College Library at Lexington. His subject was Syphilis.

In 1830, he moved to Clinton, Mississippi, where he was so successful in practice that, due to lack of time, he turned down an appointment from the Secretary of War as superintendent of vaccination among the Choctaw and Chickasaw Indians.

Submitted 18 February 1965.



*Wm. M. Gwin*

He gave up the practice of medicine in 1833. President Andrew Jackson, a close friend of his father, started him on his political career by appointing him U.S. Marshal for Mississippi. He also became a close and confidential friend of the President, visiting him every summer in Washington or in Tennessee. Gwin's circle of friends was wide. Among them was General Sam Houston. In General Houston's fight for the independence of Texas from Mexico, Dr. Gwin acted as liaison between Houston and President Jackson. He was called to Washington often for his advice and comments on various matters, especially on the annexation of Texas to the United States. He served one term, from 1841-1843, as representative in Congress for Mississippi. Following this, President James Polk appointed him commissioner to oversee the construction of the custom-house in New Orleans. In 1849, he resigned as Commissioner and decided to go to California. In Washington, he confided to Stephen A. Douglas his plan to work to make California a state and then return to Washington as its Senator.

Dr. Gwin was a rare kind of '49er. He came to California not to mine gold but for the express purpose of entering politics. In this department, he was unquestionably without a peer and his po-



litical abilities were immediately recognized. He campaigned vigorously in San Francisco and within 60 days after landing in that city was elected a member of the Constitutional Convention which met at Monterey in the fall of 1849. One delegate to the convention referred to him as the "California Machiavelli." In spite of his Southern background, he worked at the convention to adopt the Bill of Rights which prohibited slavery in the new state. He believed that the institution of slavery was an oppression to the whites among whom it prevailed.

The first California legislature assembled at San Jose on 15 December 1849, and elected its first two Senators. General Fremont was chosen on the first ballot. His term was to be for one year. On the next ballot, Dr. Gwin was chosen for the long term of six years.

He immediately went to Washington and directed all of his energies to having California admitted to the Union. There were numerous debates and conferences due to the many problems to be resolved, especially sectional rivalries and the question of slavery in the new state and the question of territorial status before statehood. On 9 September 1850, chiefly as a result of his unceasing efforts, California was admitted as a state and the next day the new senators and representatives were sworn in.

There was no question that he was California's most conspicuous and able representative in Washington. However, his political enemies condemned him for not being a true Californian and for having Southern sympathies.

Actually, Dr. Gwin was as much a Californian as any other '49er. His record amply proved he had California feelings and interests at heart. His entire activity belied the accusations that he did not work for California.

Within nine months of assuming office as Senator in Washington, he had offered 18 elaborately prepared bills into Congress for the benefit of California. At the second session of the Congress, Senator Fremont did not take his seat during the entire session and Gwin was the sole representative of California in the Senate. He not only introduced numerous bills for the interests of California, but guided them through to ultimate passage. Just a few of the more important bills involved the following: the establishment of a branch mint in San Francisco, the setting up of customs offices, location of lighthouses, erection of hospitals, sur-

veys of the port of San Francisco, deepening of the Sacramento and San Joaquin rivers, a navy yard, a naval supply depot, railroads, ocean mail steamer lines, a reduction in postage on letters and newspapers to California, establishment of an office of homestead affairs, settlers' rights, Indian affairs and circuit courts. In January 1853 he introduced a bill to authorize the construction of a Pacific Railroad. However, passage of the bill was lost in the ensuing conflict of interests of the Northern and Southern senators as to the route it was to follow. He continued to work at a solution. In 1860 he introduced a compromise bill leaving the choice of a route open. Due to the over-riding problems of secession and slavery, the compromise bill was never called to the floor.

Gwin's chief political enemy was David C. Broderick. Broderick who was in the State Legislature, wished desperately to become a U.S. Senator. He was a Northerner who came to California about the same time as Gwin and who also stepped into politics almost immediately on arriving. He not only led the opposition faction, but detested Gwin personally. He looked upon him as a wicked proslavery aristocrat and called him a "silk-socked Southern tyrant."

Broderick was a man of considerable political influence. The legislature that convened in January 1855 was to take up the question of Gwin's reelection. Broderick threw every obstacle in the way. Although 50 ballots were taken, Gwin could not muster the 56 votes necessary for reelection and his seat was vacant for almost two years. Although Broderick could not win, he kept Gwin out. It was not until January 1857, when both Senate seats would be vacant in March, that Gwin made a deal with Broderick and both were elected. In the deal, Gwin relinquished all federal patronage in California to Broderick. When Broderick was killed in a duel with Chief Justice Terry of the California Supreme Court in 1859, Gwin received some of the blame although he actually had nothing to do with it. The incident did much to accentuate and perpetrate the belief that he was a vicious proslavery politician. In spite of this ill feeling, he continued faithfully and effectively to serve California in Washington.

An unenviable task which was misunderstood by many was his service as liaison between Seward and Lincoln on the one hand and Southern secessionist leaders on the other in trying to obtain a peaceful solution before hostilities broke out. The

failure of his services in this mission added to the fuel of his enemies.

He finished his term in March 1861 and returned to California.

Dr. Gwin's career following his departure from office was clouded by the Civil War. In the fall of 1861 he was arrested on board the steamer *Ori-zaba* as the ship approached Panama after leaving San Francisco. Gwin was accused of carrying secret documents containing information about harbor defenses and the strength and disposition of the Union troops on the Coast. He was taken to New York and charged with treason but the case was dismissed for lack of evidence.

In 1863 he went to France to interest Napoleon III in a scheme for colonizing Sonora in Northern Mexico with Americans and exploiting its silver and gold mines. Napoleon and Maximilian, who was leaving to become Emperor of Mexico, favored the plan. Napoleon hoped that by colonizing the northern part of Mexico he could obtain sufficient gold and silver from its mines to pay off much of France's financial obligation. However, Maximilian lost interest in the colonization plan shortly after his arrival in Mexico. Dr. Gwin journeyed to Mexico but could not get Maximilian's cooperation. He again returned to Paris to obtain Napoleon's support. However, as the Union was winning the Civil War in the United States and Mexican opposition to Maximilian and the French continued, Dr. Gwin had to give up. Many Southerners had hoped that Gwin would be successful and that they could settle in Northern Mexico. The Confederate sympathizers, especially the "Knights of the Golden Circle," hoped to use it as a base and expected Dr. Gwin to lead them northward from Sonora to invade California and unite it with the Confederacy. However, Dr. Gwin had no such intentions.

General U. S. Grant had a different opinion. In a letter dated 8 January 1865 to Major General I. McDowell, Commanding Dept. of Pacific at San Francisco, he wrote:

"It is known that Dr. Gwin, former U.S. Senator from California, has gone to Mexico and taken service under the Maximilian Government. It is understood also that he has been appointed Governor-General of Sonora. The Doctor is a rebel of the most virulent order. His being formerly a resident of California and now getting to that State in Mexico bordering on the State of his former residence portends no good to us. May it

not be his design to entice into Sonora the dissatisfied spirits of California and if the opportunity occurs, organize them and invade the State?

"Watch this matter closely and should you find these apprehensions well founded, prepare to meet them. You will find no difficulty in raising any number of volunteers that may be necessary in California to repel an invasion of the State. Especially will this be the case when invasion comes from a country with which we are at peace."

In 1868, Dr. Gwin returned to California and lived in obscurity with his friends and family. His chief interest was in mining properties. He returned to politics only once and then in a minor role. He was a delegate to the State Democratic Convention held in San Francisco in June 1872, when he was elected delegate to the National Convention.

On a trip east to promote a railroad across Nicaragua, he died in New York City, 4 September 1885, at the age of 80.

He did not practice medicine after 1833. In politics, he was a Jackson Democrat, opposed to nullification in Calhoun's time and opposed to secession at a later date. Apparently due to the hatreds and highly charged emotional tensions of the times preceding and during the Civil War, his personal views on secession, slavery and war were deliberately misrepresented or never fully understood.

Dr. Gwin was married in December 1828. He was the father of three children by this marriage. His wife and children died in 1833. In March 1837, he married for the second time. Of the five children born to this marriage, three survived him. His descendants still live in San Francisco.

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# CASE REPORTS

## Hypoproteinemia and Cystic Fibrosis

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INADEQUATE INTAKE of protein or renal disease account for the majority of instances of hypoproteinemia and edema in infancy.<sup>1</sup> Edema as a result of hypoproteinemia is a rare occurrence in patients with cystic fibrosis of the pancreas.

Fleisher and coworkers reported four cases and reviewed 22 additional instances of hypoproteinemia and edema in children who had cystic fibrosis of the pancreas; they implicated human milk or soybean milk feedings as factors responsible for hypoproteinemia in infants with cystic fibrosis.<sup>2</sup> In the majority of reported cases, pulmonary infections and anemia developed and the patients died between eight and 16 weeks of age.

In the present case, the patient had hypoproteinemic edema at seven and a half months of age and there were other atypical features of cystic fibrosis.

### Report of a Case

A 33-week-old Caucasian girl was admitted to UCLA Hospital on 3 December 1964, because

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Submitted 4 May 1965.

of swelling of the face for one week and swelling of the legs for two days. Her health had been deteriorating since an episode of moniliasis one month before admission, which had been successfully treated.

The patient weighed 5 pounds 13 ounces at birth after an uneventful 37-week gestation and 18 hours of labor. Vertex delivery was difficult and the baby did not cry spontaneously at birth. She was in an isolette for three days with "respiratory problems," but results of roentgen and blood studies were not abnormal.

After one month on breast milk alone, the baby weighed only 5 pounds 14 ounces. When changed to cow's milk formula, the infant had considerable spitting up, wheezing, gagging and frequent loose stools. Her diet was changed to soybean-base formula at four months of age.

The patient had become increasingly irritable and anorexic after the bout of thrush at 29 weeks of age. There was colicky pain associated with passage of one large bulky stool daily. When questioned, the mother stated the stools were usually foul-smelling and sometimes floated on water. A week before the baby was admitted to hospital the mother noted puffiness of the eyelids and cheeks. When the extremities became edematous and the parents noticed the baby was urinating less frequently, her physician recommended that she be put in hospital immediately.

Many paternal relatives had asthma and "respiratory" problems. The only sibling, a 2½-year-old brother, had had two bouts of pneumonia (at seven months and 24 months of age), plus severe diarrhea and wheezing at age nine months. Although results of three sweat tests during his stays in hospital were equivocal, his present health was excellent.

The patient had puffy cheeks and pitting edema

of all extremities. The skin was pale. The pulse rate was 160. She could not sit unaided and was so irritable that she preferred to lie undisturbed on her back.

Results of blood cell count and urinalysis were within normal limits. Hemoglobin was 13.2 gm per 100 ml. Roentgenograms ruled out infantile cortical hyperostosis. Serum protein was diminished; the albumin:globulin ratio was 1.9:1.4 gm per 100 ml. The electrophoretic pattern was normal. Serum glucose, alkaline phosphatase, electrolytes, calcium, phosphorus and creatinine were within normal limits. Serum copper was borderline low. The glucose tolerance curve was normal. Three stools had greatly increased fat and starch content, were negative trypsin activity and had a pH of 6.5. A stool was negative for enteropathogens. Sweat chlorides were 116 and 142 mEq per liter by the body-bagging technique.<sup>8</sup> Repeat value by the iontophoresis method<sup>4</sup> was 111 mEq per liter.

A regimen of Viokase® with each feeding and a high protein diet with skim milk and multivitamins was begun. The edema subjectively improved, appetite increased and the child became much less irritable after five days of treatment.

One week after she was discharged from the hospital, pneumonitis developed. Throat culture showed a predominance of *Neisseria* and *Staphylococcus aureus*; chlortetracycline therapy (30 mg per kilogram of body weight per day, with good response. At 10 months of age the child was eating well and had no edema. She was continued on a high-protein, high-calorie diet, multivitamins, Viokase® and chlortetracycline.

## Discussion

This patient is unusual in that she presented with edema at seven months of age. In only three of the 26 reported cases<sup>2</sup> did the onset of edema occur later than six months. In contrast to our patient, the majority of these infants were also anemic when the diagnosis was established.

While the pathogenesis of anemia is unknown in cases of hypoproteinemic edema, intracellular copper and protein are important to the bone marrow in erythropoiesis: copper as a metal in enzyme and cytochrome structure, protein for new cell synthesis. Serum copper can be low in cases of severe edema, but this does not reflect the total body content of copper and cannot be directly related to anemia.

The diagnosis of cystic fibrosis was made in this patient at the time of severe edema and low serum protein. It has been reported that two infants with cystic fibrosis of the pancreas had normal sweat chlorides while they were edematous and hypoproteinemic.<sup>5</sup> The explanation of this phenomenon is unknown but must be related to the basic problem of hypoproteinemic edema. Edema is usually produced by a relative reduction in the osmotic pressure of plasma proteins in relation to the hydrostatic pressure in the capillaries. It is said that edema appears when the serum albumin concentration falls below 2.5 gm per 100 ml.<sup>6</sup>

Hypoalbuminemia in children with mucoviscidosis may be the result of an increased plasma volume linked to congestive heart failure.<sup>7</sup> Pittman and coworkers studied only three children, however, and they tried to correlate *in vivo* findings of increased plasma volume with rather tenuous postmortem changes suggestive of heart failure. Except for edema, there was no evidence of heart failure in the present case.

At 33 weeks of age this patient's gammaglobulin concentration was 170 mg per 100 ml; the accepted physiologic, low-normal gammaglobulin levels of infancy are 200 to 400 mg per ml. In the defense mechanisms to fight infection, the relative production and destruction of serum gammaglobulins and the types ( $\gamma^A$ ,  $\gamma^G$  or  $\gamma^M$ ) of globulins are more important factors than absolute serum gammaglobulin measurements.<sup>9</sup> Thus, we cannot say hypogammaglobulinemia or hypoproteinemic edema of cystic fibrosis specifically lowers one's defenses against infections.

The patient in the present case had difficulty in her first month of life on breast milk, as well as the serious edema while on soybean-base formula. Nitrogen balance studies have shown that soybean-base formula and breast milk are poor sources of protein for an infant with cystic fibrosis of the pancreas.<sup>3</sup> The pathogenesis of hypoproteinemia in this patient is most likely related to failure to absorb significant nitrogen from soybean milk or breast milk. Decided reduction of edema followed the institution of a high-protein diet, skim milk and oral pancreatic enzymes.

Hypoproteinemic edema and cystic fibrosis are likely to become an increasingly common iatrogenic entity. The physician dealing with feeding difficulties of infancy should not substitute soybean-base formula or continue breast milk feeding without realizing that the infant with cystic



fibrosis will develop life-threatening hypoproteine-mic edema.

## Summary

A diagnosis of cystic fibrosis of the pancreas was made in a 33-week-old infant who presented with hypoproteine-mic edema. The pathogenesis and complications of hypoproteine-mia were discussed.

Department of Pediatrics, U.C.L.A. School of Medicine, Los Angeles, California 90024 (Nebert).

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## EDITORIAL

### The Casey Bill

ASSEMBLY BILL 5, better known as the "Casey Bill," which became California law on 15 November 1965, has a great potential to provide improved medical care for California's needy, of all ages. Most of its medical provisions, including use of the prepayment mechanism, were proposed and supported by the California Medical Association. Opportunities for effective use of the law are excellent. Its concepts must now be translated into practice.

The vast new program will be administered by the California State Health and Welfare Agency, headed by Mr. Paul Ward. Mr. Ward has shown himself to be keenly aware of the problems involved in good medical practice, and to be sympathetic toward the physicians who provide it.

The law enables the state to take full advantage of the increased federal funds made available by Title XIX of Public Law 89-97. Under A.B. 5, the state can prepay medical care costs for more than 900,000 public assistance recipients and for an estimated 200,000 "medically indigent" persons (who, though they do not need other forms of public assistance, still cannot pay the essential costs of their own medical care).

California is the first state in the union to enact such far reaching legislation. It offers to California physicians an unusual opportunity to help in redesigning and improving a state welfare medical care program.

The law establishes a 16-member Health Review and Program Council, with appointments to be made by the Governor. Five members must come from the health professions, and CMA has

already submitted its nominations. This Council will have broad advisory authority to see that the most efficient possible use is made of available health care facilities and personnel—a matter of crucial importance in our rapidly growing population—and to plan for a comprehensive program of medical care for all medically indigent persons by 1975. Mr. Ward has made it clear that this Council will not be window-dressing. He intends to seek and to follow its detailed advice on all the problems that are sure to arise.

The program will begin on 1 March 1966; its prepayment provisions will begin on 1 January 1967. A very important problem is to coordinate the benefits of this law with those of the new federal health insurance program under Title XVIII of P.L. 89-97, which go into effect 1 July 1966. Getting all the gears to mesh will take a very high order of administrative skill, and maximum understanding from physicians, hospitals and prepayment agencies.

The CMA has an intense interest in the important medical provisions included in the state law. For example, to the extent feasible, medical care will be financed under a prepayment concept, long advocated by the CMA, through contracts with carriers of prepaid medical care coverage. This will allow eligible persons to secure basic health care in the same manner employed by the public generally, without discrimination or segregation based purely on their economic disability. This concept has been widely discussed as putting these eligible persons back into the "mainstream" of medical care in California. It is confidently anticipated that the effect will be an increasing tendency to provide care for such persons in the private offices of physicians and in the beds of community—rather than charity—hospitals. The flex-



ibility of such arrangements, making care available in the neighborhood where the person lives and offering increased opportunity to provide a high standard of medical care for all people who need help, is among the most promising features of this legislation.

The law provides authority for the board of supervisors of each county to integrate the county hospital services with those of other hospitals in a system of community services which offers free choice to those requiring hospital care. Again, the intent is to eliminate discrimination or segregation based on economic disability. All hospitals in the community will thus share in providing services to paying patients as well as to those who are being helped by public medical care programs. This integration of county hospitals into the total hospital resources of the community, available to all patients, is in keeping with the recommendation of the recent CMA study and report on the "Future Role of the County Hospital in California."

Payments to physicians will be based on the "reasonable charge." In determining the reasonable charge there shall be taken into consideration the customary charge for similar services generally made by the physician, as well as prevailing charges in the locality for similar services. The CMA believes that this concept is very close to its own—long sponsored—proposals of usual, customary and reasonable fees for physicians in public medical programs.

The groundwork for A.B. 5 has been solidly constructed. With good will and effort, the building can be strong and useful. It will be welcomed by all physicians as an opportunity to extend and

fulfill their pledge of a high quality of medical care for all persons, regardless of ability to pay. The law challenges each physician to read and to understand all its provisions, to remain alert to its applications, to provide—for every needy person—readily available and accessible medical care services of a very high standard of quality, and to supply those services on a basis of continuing personal concern which will make them acceptable and welcome by the people to be served.

RALPH C. TEALL, M.D.

## California's New Director of Public Health

WITH THE APPOINTMENT of Dr. Lester Breslow as Director of the California State Department of Public Health, we look forward to a continuation of the good understanding and close cooperation between the Department and the California Medical Association that in the past has well served a purpose common to both organizations—good health for the people of California.

There is good foundation for expectation that we will have sustained rapport with the Department, for in the almost twenty years that Dr. Breslow has been an executive there he has worked closely with the CMA on many studies and projects of mutual interest.

We congratulate him on his elevation to the directorship of the Department. We welcome his continued cooperation and we offer ours to him.



# California Medical Association



## NOTICES AND REPORTS

### Council Meeting Minutes

*Tentative Draft: Minutes of the 515th Meeting of the Council, Airport Marina Hotel, Los Angeles, October 30-31, 1965.*

The meeting was called to order by Chairman Anderson in the Airport Marina Hotel, Los Angeles, on Saturday, October 30, 1965, at 8:45 a.m.

#### Roll Call

Present were President Teall, President-Elect MacLaggan, Speaker Quinn, Vice-Speaker Telford, Secretary Hosmer and Councilors Isenhour, Wilson, Melone, Todd, Gooel, Taw, Bullock, O'Connor, Ham, Rogers, Burnett, Miller, Richard S. Wilbur, Watts, Fenlon, Kay, Kaiser, and Anderson. Absent for cause, Editor D. L. Wilbur, Councilors Maguire, Yant, Grunigen, Shaw and Doyle.

A quorum present and acting.

Present by invitation were Messrs. Hunton, Thomas, Clancy, Collins, Whelan, Klutch, Clark, Moreillon, Eberlein, Bowman, Goldman and Blackley, Miss Price and Mrs. Redfern of CMA staff; Mr. Robert Garrick, consultant; Messrs. Hassard and Huber, legal counsel; component society executives Scheuber of Alameda-Contra Costa, Rideout of Butte-Glenn, Geisert of Kern, Lingerfelt of Fresno, Baker of Los Angeles, Blankfort of Marin, Sommerville of Napa, Blough of Orange, Dochterman of Sacramento, Nute of

San Diego, Neick of San Francisco, Marvin of Santa Barbara, Wood of San Mateo, Donovan of Santa Clara, Monnich of San Joaquin, York of Sonoma, Whitehall of Stanislaus and Bruce of Tulare; Doctor Harold Erickson, acting director of public health; Doctor Robert T. Hewitt of the State Department of Mental Hygiene; Doctor Richard Young, medical director of the State Department of Rehabilitation; Doctor Lester McDonald, medical director of the State Department of Social Welfare; Mr. Paul Ward, administrator of the State Health and Welfare Agency; Mrs. Lois Bower, president of the Woman's Auxiliary; Mrs. Jeannette Gentili, president of the California Medical Assistants Association; Doctor William Thompson and Messrs. Potloff, Wahlberg and Bentley of California Physicians' Service; Robert Thomas, president of the California Hospital Association; Richard Layton of AMPAC; Jerry Gould of AMA field staff; Doctors Samuel R. Sherman, T. Eric Reynolds, Donald Abbott, Nicholas V. Oddo, John W. Flaiz, Henry Eastman, Dwight H. Murray, Wayne Pollock, Franz Bauer, Laurance A. Mosier and others.

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RALPH C. TEALL, M.D. . . . .	President
JAMES C. MACLAGGAN, M.D. . . . .	President-Elect
WILLIAM F. QUINN, M.D. . . . .	Speaker
JOSEPH W. TELFORD, M.D. . . . .	Vice-Speaker
CARL E. ANDERSON, M.D. . . . .	Chairman of the Council
ALBERT G. MILLER, M.D. . . . .	Vice-Chairman of the Council
MATTHEW N. HOSMER, M.D. . . . .	Secretary
DWIGHT L. WILBUR, M.D. . . . .	Editor
HOWARD HASSARD . . . . .	Executive Director

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### 1. Minutes for Approval

On motion duly made and seconded, minutes of the 514th meeting of the Council, held 18 September 1965, were approved with the following correction: Item 14, page 6, line 6 to read: "\$10,000 from a previously appropriated federal grant to the Hospital Planning Commission of Southern California would be available. . . ."

### 2. Membership

(a) A report of membership as of 27 October 1965, was presented and ordered filed.

(b) On motion duly made and seconded in each instance, 17 applicants were voted election to Associate Membership. These were: Henry N. Ricci, J. A. Rodriguez, Livia Ross, E. L. Schoenfeld, Alameda-Contra Costa County; Nathan J. Barlow, Kenneth L. Cohen, John Glenn Hazen, Esther B. Herrell, Jesse L. Herrell, Stanley J. Majcher, Merle H. Peterson, Los Angeles County; James Frederick Walker, Jr., Marin County; Frank A. Bryant, John R. Mitchell, Napa County; Richard I. Fukumoto, Orange County; George M. Plagens, Charles E. Sutton, Ventura County.

(c) On motion duly made and seconded in each instance, nine members were voted election to Retired Membership. These were: M. C. Blender, Rudolph Neustadter, Alameda-Contra Costa County; William Paul Cook, Los Angeles County; Ira J. Brandfield, Riverside County; Raymond C. Hall, O. S. Parrett, San Diego County; Karl Fleischmann, San Francisco; Ruth Martin, San Joaquin County; John J. Wells, Santa Clara County.

(d) On motion duly made and seconded, a reduction of dues was voted for 22 members for reasons of prolonged illness or postgraduate education.

### 3. Report of the President

President Teall reported on visits he had made since the last Council meeting. These included several component medical societies and their branches, the Woman's Auxiliary, the California Society of Internal Medicine, the California Hospital Association and conferences with the Conference of County Welfare Directors and with Hon. Jesse Unruh, Speaker of the State Assembly.

Doctor Teall also reported that the facilities of the California Medical Education and Research Foundation had been offered to the joint committee on the deBakey program as the fund-holding

organization for applying for a grant for planning purposes under the deBakey Law. The joint committee represents the CMA, California Hospital Association, State Department of Public Health, the deans of medical schools, the American Cancer Society, California Division, and the California Heart Association.

Doctor Teall reported on a meeting the previous evening on the Task Force on Public Law 89-97. The Task Force suggested that the Association urge Doctor James Z. Appel, president of the American Medical Association, through Dr. Gardner, secretary of HEW, to urge the Public Health Service and the Bureau of Family Services to seek consultation with practicing physicians on the implementation of those parts of Title XVIII and XIX of P.L. 89-97 assigned to the Public Health Service and the Bureau of Family Services of the Department of HEW.

**ACTION:** *Approved request to Doctor Appel to seek to secure consultation with practicing physicians by U.S. Public Health Service and HEW Bureau of Family Services on implementation of section of Public Law 89-97 assigned to those divisions.*

Finally, Doctor Teall reported on the many amendments added to Assembly Bill No. 5 by Assemblyman Casey but pointed out that the major points of interest in the measure remained unchanged. He also reported on the "Cal Med" program proposed by Assembly Speaker Jesse Unruh and on a conference held with Mr. Unruh.

**ACTION:** *Approved Committee for Emergency Action serving as liaison committee with Mr. Unruh, to study this proposal and report back to the Council.*

### 4. Introduction of Guests

The chairman introduced a number of guests at the meeting, including Mrs. Lois Bower, president of the Woman's Auxiliary, and Mrs. Jeanette Gentili, president of the California Medical Assistants Association, and Mr. Jerry Gould, AMA field staff representative.

Doctor Anderson also reported on the illness of Doctor James C. Doyle, immediate past president, on the accidental injury sustained by Doctor Dan O. Kilroy, legislative chairman, and the recent death of Doctor Edward N. Ewer, CMA president in 1925.

**ACTION:** *Voted to extend sympathy to Doctor Doyle and his family.*

**ACTION:** *Voted to extend greetings and wishes for recovery to Doctor Kilroy.*

**ACTION:** *Voted that adjournment of this meeting*

*be in the memory of Doctor Edward N. Ewer and that his family be so notified.*

#### *5. Report of President-Elect*

Doctor MacLaggan reported on his attendance at the dinner given in honor of Doctor Malcolm Merrill, retired as State Director of Public Health, and at several component society meetings.

#### *6. Report of Finance Committee*

Doctor Kay, chairman, reported that the Finance Committee would meet 17 November on the initial draft of the 1966-1967 budget and solicited suggestions from Councilors on the items to be included.

#### *7. Bureau of Research & Planning*

Doctor Sherman, chairman, recommended approval of a \$5,000 appropriation to a pilot study, through data processing, on various facets of hospital planning. This subject was referred to the Bureau from the preceding Council meeting.

***ACTION: Voted approval by required three-fourths vote, for appropriation of \$5,000 for participation with California Hospital Association and others in a pilot study on hospital planning.***

Doctor Sherman also recommended that the Commission on Medical Services be requested to compile information on the type and extent of pre-paid health care insurance available to the public to provide health care coverage for areas in Public Law 89-97 where deficiencies may exist. He proposed that consultation be had with CPS, the Health Insurance Council, Blue Cross and others for the purpose of producing a joint statement which could be disseminated to the profession and the public.

***ACTION: Voted to refer to the Commission on Medical Services the question of developing material to point to areas where health care coverage may be desirable to supplement the provisions of Title XVIII of Public Law 89-97. Commission to report back to the Council.***

***ACTION: Voted that Commission on Medical Services report to the Council no later than the next meeting on the advisability of preparing, in conjunction with CPS, the Health Insurance Council, Blue Cross and others, a statement for public dissemination on the areas where supplementary health care coverage to Public Law 89-97 may be advisable.***

Doctor Sherman also reported that the Bureau was contemplating meetings with representatives of component societies in whose jurisdiction may be found identifiable areas of disadvantaged population, such as the Watts area of Los Angeles and

the Hunter's Point area of San Francisco, for the purpose of stimulating these societies in pointing out to the people involved the availability of health care programs maintained under various programs, or in developing mechanisms and programs through which health care services can be provided.

***ACTION: Voted to approve the concept suggested by the Bureau of Research & Planning and to send a statement to the component societies in regard to this proposal.***

A further recommendation was that the Commission on Medical Services be requested to bring up to date the study on "Components of Adequate Health Care Coverage" which was presented several years ago to the Council and the House of Delegates.

***ACTION: Voted to request Commission on Medical Services to update the study on "Components of Adequate Health Care Coverage."***

Doctor Sherman also asked authority for the bureau to cooperate with California Physicians' Service in a pilot study in several self-selected counties to determine the methodology to be used in securing usual and customary fees which would be helpful in establishing physician profiles and prevailing fees.

***ACTION: Bureau of Research & Planning authorized to proceed cooperatively with California Physicians' Service, CMA's fee committee and others in planning for a pilot study to determine the usual and customary fees of physicians and the methodology for securing these findings, and to report back to the Council on the proposed format of such a study.***

The bureau also asked authority to distribute copies of the Second Progress Report of the Committee to Study the Role of Medicine in Society to officers of medical societies in other states and others who had requested copies. A question was raised as to whether or not the requirements of the House of Delegates on distribution of this report had been complied with.

***ACTION: Voted to authorize distribution of copies of the Second Progress Report of the Committee to Study the Role of Medicine in Society, on request, without further approval of the Council. Each copy so distributed to carry the notation that it is sent as a sociological study of the CMA but does not represent official CMA policy.***

***ACTION: Voted that staff distribute copies of the Second Progress Report of the Committee to Study the Role of Medicine in Society to all component societies, with a request that they register their reaction to distribution of the report prior to the 1966 House of Delegates meeting.***



#### 8. *State Health and Welfare Agency*

Mr. Paul Ward, Administrator of the State Health and Welfare Agency, reported on the current status of Assembly Bill No. 5, which would expand the Medical Assistance to the Aged program and would introduce the concept of prepayment for medical services under this program. The measure has passed the Assembly, he said, and is now in a Senate Committee where it is due for early hearing. Some proposed amendments, he reported, would eliminate the prepayment and other concepts of the original measure. He urged that this measure be followed closely in the immediate future.

#### 9. *State Department of Public Health*

Doctor Harold Erickson, acting director of the State Department of Public Health, reported that the department is studying its responsibilities under Public Law 89-97 in the certification of hospitals and extended care facilities.

Doctor Erickson also reported that the State Board of Health had recently adopted regulations pertaining to PKU testing, parakeets, the redirected alcohol control program and smog. Copies of these regulations will be sent to Councilors and to component societies.

#### 10. *State Department of Social Welfare*

Doctor Lester McDonald, medical director of the State Department of Social Welfare, distributed copies of a report on the medical care programs of the department and commented on the reductions made, for cost reasons, in the drug formulary. The department, he said, is experiencing difficulty in the case of telephoned prescriptions.

#### 11. *State Department of Rehabilitation*

Doctor Richard Young, medical director of the State Department of Rehabilitation, reported that Public Law 89-97 will make additional federal funds available for rehabilitation programs and that the program of the Department of Vocational Rehabilitation would be practically doubled. He also introduced Doctor Seymour Kolko who has been retained as a psychiatric consultant to the department.

#### 12. *State Board of Medical Examiners*

Doctor Donald Abbott, immediate past president of the State Board of Medical Examiners, re-

ported that all nominations from the board, from medical school deans and from the CMA for appointments to district disciplinary review boards have reached the Governor.

Doctor Abbott also reported that the board has developed a report form to be used in the periodic reports of all licensed general and specialized hospitals to the board under new legislation. Copies of the covering letter and the report form will be made available to Councilors and component societies.

Doctor Abbott also reported that the board had agreed that a special medical agent who must be a licensed physician and surgeon should head the new areas of responsibility, including gross incompetence, gross immorality, gross negligence and mental illness, and has recommended to the Department of Professional and Vocational Standards the attributes deemed necessary in selecting a physician to handle this assignment.

Doctor Abbott also reported that at the annual meeting of the board Doctor Nicholas V. Oddo of Long Beach had been elected president, Doctor Robert C. Combs of San Francisco vice-president and Doctor Shelby M. Hicks of Merced secretary.

#### 13. *California Hospital Association*

Henry Jackson, president-elect of the California Hospital Association, reported on the recently held annual meeting of the association, at which the principal topics of discussion were Public Law 89-97, the deBakey program and the Casey Bill (AB 5) now pending in the state legislature. He also reported that the association has opened an office in Sacramento for improved service to its members.

#### 14. *California Physicians' Service*

Doctor William Thompson, board chairman of California Physicians' Service, gave a progress report on CPS activities, including several meetings held for discussion of the implications of Public Law 89-97.

#### 15. *Medical Executives Conference*

Mrs. Olive Neick, chairman of the Medical Executives Conference, reported on the meeting held 29 October, at which the California physicians serving on several advisory committees on Public Law 89-97 had discussed their programs and accomplishments.

## 16. *California Volunteers for Political Action*

Doctor Malcolm Todd, chairman of Calpak, reported that a meeting had been held the previous week and invited all members of the Council to attend a meeting scheduled for 13 November in San Francisco, at which several outstanding speakers will appear. He urged continued support of the Calpak and AMPAC movements.

## 17. *Commission on Medical Services*

Doctor Ralph Burnett, reporting for the Commission on Medical Services, reviewed a number of resolutions referred to the Commission following the 1965 House of Delegates meeting. On several he asked Council action, including the following:

*Resolution 24-65*, relating to insurance coverage for intensive hospital care where essential for good medical care. The Commission noted its approval and its desire to send copies of the resolution to all insurance carriers in the state.

**ACTION:** *Commission's plans approved by Council.*

*Resolution 27-65*, relating to disability benefits. The Commission reported its lack of knowledge in this field and suggested referring the resolution to the Committee on Occupational Health and Rehabilitation.

**ACTION:** *Resolution 27-65 voted referred to Committee on Occupational Health and Rehabilitation.*

*Resolution 32-65*, relating to Over 65 health insurance, the commission reported its feeling that the achievement of a single insurance package of comprehensive coverage was not feasible.

**ACTION:** *Resolution 32-65 referred back to Commission on Medical Services for further study.*

## 18. *Committee on Legislation*

Mr. Ben Read reported on the status of the legislation remaining in the hands of the State Legislature at this time and on the proposed handling of interim committee referrals in the Senate and the Assembly.

## 19. *Commission on Community Health Services*

Doctor Kay, chairman of the Commission on Community Health Services, presented a report containing several informational items and some on which Council action was sought.

**ACTION:** *Voted approval of the commission's plans to participate in a statewide conference with other state agencies and the Committee on Rural Health on health and safety for rural dwellers.*

**ACTION:** *Voted approval of a proposed statement on coordinated home care previously presented and worked out in cooperation with a hospital administrator whose hospital has been operating such a program for several years.*

Commission urged the Council to renew its efforts for professional education of the need for direct billing of laboratory fees.

## 20. *Commission on Professional Welfare*

Mr. William Whelan presented a report for the Commission on Professional Welfare, including developments on disability insurance coverage for CMA and county society executive staff members, reduced disability insurance premiums for young physicians and insurance riders for coverage of physicians flying their own airplanes.

**ACTION:** *Approved offering of disability insurance coverage to executive employees of CMA and its component societies, provided benefits are limited to 75 per cent of the annual compensation.*

## 21. *Commission on Allied Health Professions and Services*

Doctor Wayne Pollock presented the report of the Commission on Allied Health Professions and Services, relating to the services of registered nurses.

**ACTION:** *Approved commission recommendation that the induction of hypnosis is not a function in which nurses should be engaged except in assisting a doctor who is adequately trained in this technique and nurses' activities should be limited to this assistance.*

**ACTION:** *Approved commission consensus that the use of intercaths by registered nurses is customary practice, that intercaths have no different function from needles and require no different consideration when used under the orders or direction of a physician.*

**ACTION:** *Approved recommendation that anesthesiologists and chest physicians train nurses or other ancillary personnel in each hospital in intubation and extubation procedures so that a competent person is readily available to perform inhalation therapy on a 24-hour basis.*

**ACTION:** *Voted approval of nurses performing intraocular testing under the orders or direction of a physician.*

**ACTION:** *Approved a statement prepared jointly by the Commission, the California Hospital Association and the California Nurses Association on the subject of nurse procedures in acute cardiac care, subject to legal counsel's approval prior to next Council meeting.*

## 22. *Staff Report*

Mr. Hassard distributed a report on the progress of implementation of all resolutions adopted by the 1965 House of Delegates.

## 23. *Legal Department*

Mr. Hassard reported on the continuation of a



program of the Internal Revenue Service, previously reported, of giving special training to agents in the auditing of tax-exempt organizations and stated that the Association may expect such an audit some time in the future.

He also reported that regulations have been proposed but not yet issued by Internal Revenue Service to provide for taxation of nonrelated income of tax-exempt organizations from advertising income of journals and from exhibits at meetings.

Mr. Hassard also called attention to the "Model Medical Staff Bylaws" presented earlier as a joint effort by the Association and the California Hospital Association and pointed out that these bylaws provide that any applicant for membership be safeguarded as to his inherent rights in the eyes of the law. He urged that full consideration be given to this factor in all hospitals.

#### 24. *Ad Hoc Committee on Workmen's Compensation*

Doctor Anderson, chairman, reported on a meeting with officials of the Industrial Accident Commission at which the commission evidenced its desire to compile a list of physicians both qualified and interested in handling industrial injury cases. It was agreed that the Association should serve as the survey center for inquiries to all practicing physicians in the state, whether or not they are CMA members.

**ACTION:** *Approved CMA handling Industrial Accident Commission mailing to all practicing physicians in California, with employers and insurance carriers to share in the cost.*

Doctor Anderson also reported that the Industrial Accident Commission has been urged by the Association, the self-insurers and labor organizations to establish a rehabilitation unit, to act in a referral and liaison capacity to established rehabilitation facilities.

#### 25. *Examination for Drivers' Licenses*

The chairman presented a letter from a member urging that a personal physician should not be required to make a determination of the ability of his patient to obtain a driver's license but that a panel of independent medical examiners should be established to handle this procedure. After discussion it was agreed to refer the letter to the Committee on Traffic Safety.

#### 26. *Woman's Auxiliary*

Doctor MacLaggan presented the request of the Woman's Auxiliary for an additional appropriation to cover the cost of coffee supplied to those attending the annual session.

**ACTION:** *Voted additional appropriation of \$400 for Auxiliary purchase of coffee.*

#### 27. *Section on Pediatrics*

Doctor MacLaggan reported that the Section on Pediatrics has secured the agreement of the Academy of Pediatrics to hold its meeting as a part of the section's program at the next annual session. He asked that the Council express its approval.

**ACTION:** *Voted that approval be expressed for Academy of Pediatrics to hold its meeting in conjunction with the annual session program of the Section on Pediatrics.*

#### 28. *Medical Libraries*

Doctor Miller reported that the medical library assistance bill, HR 3142, has passed both houses of Congress and that efforts should be made at once to secure some of the available funds for support of medical libraries in California.

**ACTION:** *Voted to refer library support funds from federal government to the Committee on Continuing Medical Education of the Scientific Board for such coordination as may be provided to secure funds for medical libraries in California.*

#### *Recess*

At this point, 4:10 p.m. on 30 October 1965, the Council recessed until 8:00 a.m. on Sunday, 31 October 1965.

#### 29. *General Session as Committee of the Whole*

The Council discussed a number of questions in informal fashion, touching upon such matters as liaison with local and county governments, the need for physicians to participate in governmental programs, the requirements for additional staff for increased activities, the need of strengthening the Sacramento office, the need for increased communications facilities, the possible use of members of the House of Delegates as communications forces, the use of funds now contributed to the American Medical Association-Education and Research Foundation, the implications of new legislation such as the deBakey program and the need of continuing Communications efforts among the membership.

Visual material in the form of a statement on

the financial position of the Association, an outline of all staff procedures and members, lists of allied organizations, etc., was made available.

A proposal was made that the format of Council meetings be changed so that essential business could be handled at an earlier hour each day and informational material presented at a later hour. Suggestions were also presented for a curtailed luncheon period at Council meetings, for lighter luncheon items and for Councilors planning on later departures from meetings.

**ACTION:** *Voted to retain Mr. Hassard as executive director under terms initially adopted in 1958 and amended subsequently.*

**ACTION:** *Voted to authorize the retention of the services of Mr. K. L. Hamman as a consultant to the Council and the executive director on matters of finance and organizational structure.*

**ACTION:** *Voted that Mr. Hassard and the staff, in conjunction with officers and others, prepare outlines for changed or expanded programs for the Association and to bring such outline back to the Council for consideration.*

**ACTION:** *Voted that each Councilor consider the development, within his district, of a communications program involving CMA delegates and others as might be most effective in his district. CMA staff would assist in this effort upon request. Specific emphasis at this time to be on problems relating to governmental medical care programs.*

#### *Adjournment*

There being no further business to come before it, the meeting was adjourned at 2:30 p.m. in the memory of Doctor Edward N. Ewer.

CARL E. ANDERSON, M.D., *Chairman*

MATTHEW N. HOSMER, M.D., *Secretary*

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## 1965 CONSTITUTIONAL AMENDMENTS, FOR ACTION IN 1966

Under the terms of the Constitution, proposed constitutional amendments must lie on the table until the next regular meeting of the House of Delegates following the meeting at which they were introduced. A proposed amendment introduced at the 1965 meeting and to be acted upon in 1966 is presented below. In addition, one By-law amendment was introduced at the second session of the 1965 House of Delegates and, since it could not be acted upon for at least 24 hours, was held over for action in the next regular (1966) meeting.

The Proposed Constitutional amendment is required to be printed in two issues of the journal before it comes before the House of Delegates for action.

### CONSTITUTIONAL AMENDMENT 1-65

Introduced by: The Council

Subject: Composition of Council

**Resolved:** That Article III, Part B, Section 9, paragraph (c) of the Constitution of the California Medical Association be amended by deleting the words "without the right to vote" at the end of the section, so that the section will read:

"(c) One (1) member of the Executive Com-

mittee of the Scientific Board to be elected by the Executive Committee of that body from representatives of the scientific sections or members-at-large."

### BY-LAW AMENDMENT 22-65

Introduced by: Walter F. Carpenter

Representing: 1965 Reference Committee No. 2

Subject: Payment of Dues

**Resolved:** That Chapter 2, Section 10, Paragraph (b) of the Bylaws of the California Medical Association be amended by deleting the language shown below in parentheses and by adding the language shown below in italics, so that the section shall read:

"By Failure to Pay Dues. If the Annual assessments of dues, payable to this Association or the American Medical Association by any member of this Association, are not paid in full on or before (April) *March* 1, of any year, such member shall automatically lose his membership in this Association as of (April) *March* 1 of such year. The Council of this Association, in its discretion, upon payment of such unpaid dues, and any other assessments of dues accruing thereafter, may at any time reinstate such member."



## In Memoriam

BARBOUR, CONSTANCE, Berkeley. Died 27 November 1965, near Big Sur, from injuries received in an automobile accident, aged 43. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1955. Licensed in California in 1956. Doctor Barbour was a member of the Alameda-Contra Costa Medical Association.



BASSHAM, BYRON EARL, El Centro. Died 21 November 1965, in El Centro, aged 56, of heart disease. Graduate of The University of Chicago, The School of Medicine, Illinois, 1941. Licensed in California in 1950. Doctor Bassham was a member of the Imperial County Medical Society.



BROWNING, GEORGE L., Sacramento. Died 26 November 1965, in Sacramento, aged 58. Graduate of Stanford University School of Medicine, Palo Alto-San Francisco, 1940. Licensed in California in 1940. Doctor Browning was a member of the Sacramento County Medical Society.



DOEHRING, CARL FREDERIC, Altadena. Died 1 October 1965, in Altadena, aged 62, of coronary thrombosis. Graduate of Rush Medical College, Chicago, Illinois, 1928. Licensed in California in 1933. Doctor Doehring was a member of the Los Angeles County Medical Association.



EHRKE, ALBERT ADOLPH, Dinuba. Died 9 December 1965, aged 70, of heart disease. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1920. Licensed in California in 1920. Doctor Ehrke was a member of the Tulare County Medical Society.



EWENS, FREDERIC, Manhattan Beach. Died 4 December 1965, in Manhattan Beach, aged 71, of heart disease. Graduate of Jefferson Medical College of Philadelphia, Pennsylvania, 1920. Licensed in California in 1929. Doctor Ewens was a member of the Los Angeles County Medical Association.



LYON, CHESTER HAROLD, Los Angeles. Died 22 November 1965, in Los Angeles, aged 55, of coronary artery disease. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1937. Licensed in Cali-

fornia in 1937. M.D. degree from California College of Medicine, 1962. Doctor Lyon was a member of the Los Angeles County Medical Association.



MADDOX, RALPH L., Novato. Died 19 November 1965, aged 44. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1949. Licensed in California in 1949. Doctor Maddox was a member of the Marin Medical Society.



SHAW, LUTHER U., Canoga Park. Died 5 November 1965, in Los Angeles, aged 41, of intestinal obstruction, hepatic failure. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1951. Licensed in California in 1951. M.D. degree from California College of Medicine, 1962. Doctor Shaw was a member of the Los Angeles County Medical Association.



SPRAGUE, GERALD TRUE, Van Nuys. Died 11 November 1965, in Van Nuys, aged 66. Graduate of the University of Cincinnati College of Medicine, Ohio, 1925. Licensed in California in 1928. Doctor Sprague was a member of the Los Angeles County Medical Association.



STUART, HUGH ALEXANDER, San Jose. Died 19 November 1965, in San Jose, aged 60. Graduate of McGill University Faculty of Medicine, Montreal, Quebec, Canada, 1928. Licensed in California in 1959. Doctor Stuart was a member of the Santa Clara County Medical Society.



WALL, HERBERT WILLIAM, Yucaipa. Died 30 November 1965, in Redlands, aged 81. Graduate of the University of Western Ontario Faculty of Medicine, London, Ontario, Canada, 1910. Licensed in California in 1921. Doctor Wall was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



WEEDN, HENRY JOHN, Newport Beach. Died 12 November 1965, in Lakewood, aged 73, of cancer of pancreas. Graduate of the University of Oklahoma School of Medicine, Oklahoma City, 1916. Licensed in California in 1922. Doctor Weedn was a member of the Los Angeles County Medical Association.



# ANNUAL SCIENTIFIC ASSEMBLY

**MARCH 20-23, 1966**

**LOS ANGELES**

*current concepts in therapy*

**POINT AND COUNTERPOINT**

*featuring—*

**RENAL FAILURE  
CORONARY ARTERY DISEASE  
GASTROINTESTINAL HEMORRHAGE**

• *among the distinguished speakers  
presenting their "current concepts in therapy":*

- CHARLES K. FRIEDBERG, M.D., Columbia University
- BERNARD LOWN, M.D., Harvard University
- BELDING H. SCRIBNER, M.D., University of Washington
- OWEN H. WANGENSTEEN, M.D., University of Minnesota

A VARIETY OF EVENTS in addition to those directly related to this year's theme WILL HIGHLIGHT YOUR 1966 ANNUAL SCIENTIFIC ASSEMBLY . . . eighteen medical specialty section meetings . . . seven special conferences . . . motion picture symposia . . . color TV programs . . . scientific and technical exhibits.



# WOMAN'S AUXILIARY

to the California Medical Association



## AMA-ERF

### *AMA-ERF is:*

A program with a dual purpose of providing assistance to medical schools and providing funds which can be used for the betterment of public health through scientific and medical research.

A sound basis for future expansion and provides unified direction and control within the framework of a single Foundation.

A priority project of the Woman's Auxiliary to the American Medical Association.

### *Program:*

The five current projects of the Foundation involve collecting funds for: (1) Medical Schools; (2) Medical Education Loan Guarantee Program; (3) Fellowship Program in Medical Journalism; (4) Institute for Biomedical Research; (5) Research Project on Smoking and Health.

The Woman's Auxiliary at district, county, state and national levels seeks funds to support two of the Foundation's projects: (1) Funds for Medical Schools; (2) Loan Guarantee Fund.

### *Operation:*

1. Funds for Medical Schools: The Foundation provides the deans of medical schools with a source of unrestricted funds to assist in meeting the ever-increasing costs of medical education. Private support is an absolute necessity if medical education is to remain at its present high level.

2. Loan Guarantee Program: The Foundation makes it possible for medical students, interns and residents to borrow up to \$1500 a year and up to \$10,000 for an entire training period. No payments are required until five months after completion of all full-time training, including internship and residency. Medical schools and hospitals are not required to put up matching funds or to make collections. There is no limit on available funds.

Banks will loan \$12.50 for each dollar contributed to the Loan Guarantee Fund and contributions typically keep pace with loan demands.

### *Accomplishments:*

1. Funds for Medical Schools: More than \$1,208,463 was distributed in March to medical schools in the United States and Canada. Of this amount six medical schools in California received \$229,620.

2. Loan Guarantee Program: The Foundation has raised \$2,472,000 as a guarantee fund for loans. Each dollar guarantees \$12.50 in bank loans, thus providing a credit potential of more than \$30,000,000. At the rate of 600 loans per month the Foundation has approved 19,298 loans amounting to \$27,600,000. One out of every six medical students, interns and residents has received at least one AMA-ERF loan. In California alone 2,147 loans have been granted which have advanced \$2,629,050 to medical trainees (far more than in any other state).

3. Woman's Auxiliary 1964-65: (a) On a national level \$320,121.87 was contributed to the AMA-ERF. (b) On a state level California won a national award for the highest state contribution, \$45,869. (c) On a county level Los Angeles won a national and a state award for the highest county contribution with \$18,869. The San Luis Obispo Auxiliary won a state award for the highest per capita contribution, \$16.03. The Yuba-Sutter-Colusa Auxiliary won a state award for the highest percentage of increase over the previous year—212 per cent.

### *Support—Why?*

1. The AMA-ERF program is a "natural" priority project for organizations of physicians and physicians' wives, as their first concern should be the welfare of present and future physicians. Since the earliest days of medicine physicians have recognized their obligation to pass their medical knowledge and skills on to the next

generation in order to help carry medicine forward.

2. The Government Loan Program is *not* adequate. The \$30,000,000 authorized by the government for three years will not cover the present needs for loans to students of medicine, osteopathy and dentistry. Interns and residents are not included in any way in the government program.

In granting government loans a school shall give preference to persons who enter as first-year students. A further provision prohibits use of these funds in combination with National Defense Education Act funds.

Repayment of government loans begins three years after the completion of school, and in many cases this could mean that the borrower would begin repayment while still in residency.

Schools are required to put up one dollar for every nine dollars allocated by the government. Schools are also responsible for the collection of the government loans.

#### *Support—How?*

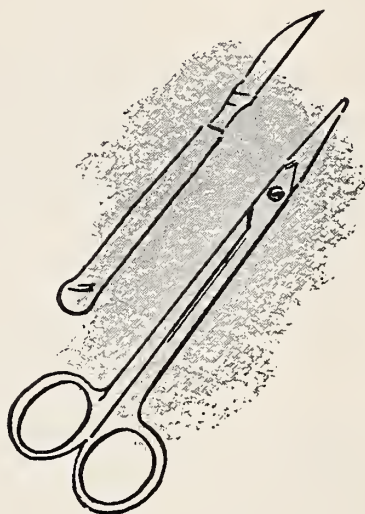
Several projects have been developed by AMA-ERF to assist as fund-raisers: sale of In-Memoriam and In-Appreciation cards, playing cards and matching score pads in a variety of colors, state and caduceus charms and bracelets in 14 karat gold and sterling silver. There are any number of local projects that have been developed and used successfully: fashion shows, rummage sales, dinner parties, dances, bridge parties, luncheons, teas, cookbook project, art exhibits.

#### *1965-66*

With the facts as outlined, before us, let us resolve here and now (both physicians and their wives) to pledge maximum support to further the program of the American Medical Association Education Research Foundation, our priority project.

MRS. VIRGIL S. CRAWLEY

*AMA-ERF Chairman, W.A.C.M.A.*





# NEWS & NOTES

NATIONAL • STATE • COUNTY

## LOS ANGELES

Dr. George C. Andersen of Hermosa Beach became president of the Los Angeles County Medical Association at the first of the year, succeeding Dr. John A. Bullis. Dr. Joseph F. Boyle, South Pasadena, was named president-elect, Dr. Neal C. Hamel, Encino, vice-president and Dr. Jean F. Crum, Norwalk, secretary-treasurer.

\* \* \*

Dr. H. Martin Engle, director of the Los Angeles Veterans Administration Center, has been named chief medical director of the Veterans Administration. He is to transfer to his new post in Washington, D.C., this month.

## SAN FRANCISCO

Dr. Melvin Malcolm Grumbach, associate professor of pediatrics at Columbia University College of Physicians and Surgeons, has been appointed professor and chairman of the Department of Pediatrics, School of Medicine, University of California San Francisco Medical Center. He succeeds Dr. Edward B. Shaw, who is retiring after forty years of service to the University.

\* \* \*

The fifth annual **Sterling Bunnell Memorial Lecture** on reconstructive surgery will be given by Dr. Daniel C. Riordan, 25 February 1966, at 8:00 p.m., in Lane Hall, Presbyterian Medical Center, San Francisco. Dr. Riordan is associate professor of clinical orthopedic surgery at Tulane University School of Medicine.

The lecture is entitled: "Tendon Transfers in the Surgical Reconstruction of the Hand and Forearm—A Critical Presentation, Discussion and Analysis."

## SANTA CLARA

Dr. Stanley A. Skillicorn, San Jose, was installed as president of the Santa Clara County Medical Society 1 January, succeeding Dr. Richard S. Wilbur, Palo Alto; and Dr. Gerald Besson of Sunnyvale was elected president-elect.

## NEW DEAN AT DAVIS

Dr. Charles John Tupper, associate dean of the University of Michigan School of Medicine, has been appointed Dean of the University of California School of Medicine at Davis, which is now in process of formation. The new dean, who is a graduate of the University of Nebraska College of Medicine, taught internal medicine



DR. CHARLES JOHN TUPPER

at Michigan for six years before becoming associate dean in 1961.

He is a fellow of the American College of Physicians and besides his administrative and teaching duties at Ann Arbor he has been active in the Washtenaw County Medical Society, which he served as president in 1964. He was a delegate to the 1961 White House Conference on Aging and last year was a member of the AMA National Speakers Bureau.

Dr. Tupper is Scientific Editor of *Michigan Medicine* and he has published widely on problems of internal medicine, including articles on duodenal ulcer in college undergraduates, a living program for senior citizens, the college professor's health and health care habits, changing trends in medical practice and automobile safety. He was co-recipient of the AMA Billings Bronze Medal for an exhibit on periodic health examinations in 1955.

The new dean will move to Davis in February to begin planning for the University's new medical school there, which is scheduled to admit its first class in the fall of 1968.

A graduate of Point Loma Junior-Senior High School in San Diego, Dr. Tupper also has a bachelor's degree from San Diego State College. He is married and has a son and a daughter.

# *16th annual regional postgraduate institute*

*OJAI VALLEY INN  
Ojai  
March 11-12, 1966*

## **WEST COAST COUNTIES**

Presented cooperatively by West Coast Counties Medical Societies, Continuing Education in Medicine and the Health Sciences, University of California San Francisco Medical Center, and the Committee on Continuing Medical Education, California Medical Association.

**HOST:** Santa Barbara County Medical Society.

**Regional Chairman:** George J. Wittenstein, M.D.,  
222 West Pueblo Street, Santa Barbara.

**INSTITUTE FEE:** \$15.00. For additional information contact Continuing Medical Education office, California Medical Association, 693 Sutter Street, San Francisco 94102. All California Medical Association members and their families are cordially invited to attend.

**GUEST SPEAKER:** Claude Welch, M.D., Clinical Professor of Surgery, Harvard Medical School; Visiting Surgeon, Massachusetts General Hospital.

## **INDICATIONS FOR SURGICAL INTERVENTION— THE DIFFICULT DECISION**

**FRIDAY, MARCH 11**

### *Morning Session*

#### **HIATUS HERNIAS**

I refer to the surgeon when—Howard Shapiro, M.D.

I feel I should operate when—Orville F. Grimes, M.D.

#### **PEPTIC ULCER**

The patient needs surgical treatment if—Hugo C. Moeller, M.D.

I would agree to operate if—Claude Welch, M.D.

#### **GALLBLADDER DISEASE**

Surgical help is necessary because—Howard Shapiro, M.D.

I would agree to surgery because—Robert Combs, M.D.

### *Afternoon Session*

#### **COLITIS, DIVERTICULAR DISEASE AND OTHER PROBLEMS IN THE COLON**

I think we have reached the point for surgery since—John Carbone, M.D.

I would agree to a surgical approach since—Walter Birnbaum, M.D.

**CONCURRENT WORKSHOPS** (you may go to one of your choice):

Case discussions: West Coast Counties participants with the faculty.

A. **Biliary System**—John Carbone, M.D., Claude Welch, M.D.

B. **Colon and Rectum**—Walter Birnbaum, M.D., Howard Shapiro, M.D.

C. **Esophagus and Stomach**—Orville F. Grimes, M.D., Hugo C. Moeller, M.D.

**SATURDAY, MARCH 12**

### *Morning Session*

#### **THE INFECTED URINARY TRACT**

Surgical assistance is necessary when—Allan M. Unger, M.D.

I agree to a surgical approach when—Donald R. Smith, M.D.

#### **NONMALIGNANT PULMONARY PROBLEMS**

I feel the surgeon can help if—Roger H. L. Wilson, M.D.

I would be willing to use a surgical approach if—Orville F. Grimes, M.D.

#### **THYROID NODULES**

Certain of these should be explored because—Francis Greenspan, M.D.

I would surgically explore these patients because—Claude Welch, M.D.

### *Afternoon Session*

#### **THE POOR RISK PATIENT**

**Cardiac, pulmonary and metabolic problems**—Walter Birnbaum, M.D., John Carbone, M.D., Robert Combs, M.D., Francis Greenspan, M.D., Hugo C. Moeller, M.D., Donald R. Smith, M.D., Allan M. Unger, M.D., Claude Welch, M.D., Roger H. L. Wilson, M.D.

**CONCURRENT WORKSHOPS** (you may go to one of your choice):

Case discussions: West Coast Counties participants with the faculty.

A. **Lungs**—Orville F. Grimes, M.D., Roger H. L. Wilson, M.D.

B. **Thyroid**—Robert Combs, M.D., Francis Greenspan, M.D.

C. **Urinary Tract**—Donald R. Smith, M.D., Allan M. Unger, M.D.



# EDUCATION NOTICES

## Meetings and Courses

### COMMITTEE ON CONTINUING MEDICAL EDUCATION

THIS BULLETIN of the dates of continuing education programs and the meetings of various medical organizations in California is supplied by the Committee on Continuing Medical Education of the California Medical Association. In order that they may be listed here, please send communications relating to your future meetings or postgraduate courses to Committee on Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco, California 94102.

#### KEY TO ABBREVIATIONS AND SYMBOLS

##### Medical Centers and CMA Contacts for Postgraduate Course Information

CMA:	California Medical Association For information contact: Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco 94102. PRospect 6-9400, Ext. 68.
LLU:	Loma Linda University For information contact: W. F. Norwood, Ph.D., Associate Dean, Continuing Education, Loma Linda University School of Medicine, 1720 Brooklyn Ave., Los Angeles 90033, ANgeles 9-7241, Ext. 214.
PRES. MED. CTR.	Presbyterian Medical Center For information contact: Arthur Selzer, M.D., chairman, Education Committee, Presbyterian Medical Center, Clay and Webster Streets, San Francisco 94115. WEst 1-8000.
UCLA:	University of California at Los Angeles For information contact: Donald Brayton, M.D., Assistant Dean for Postgraduate Medical Education, 15-39 Rehabilitation Center, University of California Center for Health Sciences, Los Angeles 90024, 478-9711, Ext. 4345.
UCSF:	University of California, San Francisco For information contact: Seymour M. Farber, M.D., Dean, Educational Services and Director, Continuing Education, University of California Medical Center, Room 565-U, San Francisco 94122, 666-1692.
USC:	University of Southern California For information contact: Phil R. Manning, M.D., Associate Dean, Postgraduate Division, USC School of Medicine, 2025 Zonal Ave., Los Angeles 90033, CApital 5-1511, Ext. 300.
STAN:	Stanford University For information contact: Roy Cohn, M.D., Associate Dean for Graduate Affairs, Stanford University School of Medicine, 300 Pasteur Drive, Palo Alto, DAVenport 1-1200.

#### JANUARY

January 15—**Childrens Hospital of Orange County Postgraduate Course. Problems of Pediatric Endocrinology.** Amphitheater Conference Room, CHOC, 1109 W. La Veta, Orange. Saturday. 8:30 a.m.-3:50 p.m. \$5. Contact: Merl J. Carson, M.D., medical director, CHOC.

January 15—**Orange County Heart Association Symposium on Heart Disease.** OCHA, 1043 W. 8th St., Santa Ana. Saturday. 6 hours. \$15. Contact: John M. Salyer, M.D., OCHA.

January 17-21—**Annual Mid-Winter Convention in Ophthalmology and Otolaryngology.** Statler Hilton Hotel, Los Angeles. Monday-Friday. Contact: Norman Jesbere, M.D., secretary treasurer, Research Study Club of Los Angeles, 1136 West Sixth Street, Los Angeles 90017.

January 18-April 12—**Medical Radio Conferences.** UCSF. Tuesdays, 12:30-1:30 p.m.

January 19—**Los Angeles County Heart Association Annual Midwinter Symposium.** Statler Hilton Hotel. Los Angeles. Wednesday. 6 hours. Contact: Professional Symposium Committee, LACHA, 2405 W. Eighth Street, Los Angeles 90057.

January 19—**Riverside County General Hospital Postgraduate Assembly.** RCGH. Wednesday. 12 hours. Contact: Harold A. Roth, M.D., RCGH, 9851 Magnolia Avenue, Riverside 92503.

January 19-April 20—**Psychotherapeutic Principles and Practice for Non-Psychiatrists.** UCSF. Wednesdays. 70 hours. \$25.

January 19-May 18—**Teaching Clinics in Psychiatry.** UCLA. Wednesdays.

January 20-21—**New and Old Antibiotics.** USC at Los Angeles County Hospital. Thursday-Friday. 16 hours. \$35.

January 20-April 7—**Medical Radio Conferences.** UCSF. Thursdays, 12:30-1:30 p.m.

January 22—**Central Mission Trails Heart Association Annual Symposium on Cardiovascular Disease.** Fort Ord Army Hospital, Fort Ord. Saturday. 8 hours. \$10. full day, \$5. half day. Contact: Donald M. Scanlon, M.D., P.O. Drawer 4948, Carmel.

January 22—**Pediatric Cardiology Symposium.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

January 22—**SAN LUIS OBISPO POSTGRADUATE COURSE** presented by California Medical Association in cooperation with Stan. San Luis Obispo Country Club, San Luis Obispo. Saturday. \$7.50. Chairman: Henry A. Zevely, M.D., 100 Casa Street, Suite C-2, San Luis Obispo.

January 28—**Nuclear Medicine, Part I.** USC at Los Angeles County Hospital. Friday. 20 hours. \$60.

January 28-30—**Clinical Conference in Pediatric Anesthesiology.** Friday-Sunday. Contact: M. Digby Leigh, M.D., Childrens Hospital of Los Angeles, 4614 Sunset Blvd., Los Angeles 90027.

January 28-30—**Dermatologic Pathology.** USC at El Mirador Hotel, Palm Springs. Friday-Sunday.

January 29—**Practical Proctology.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

January 29-30—**Los Angeles Radiological Society Annual Midwinter Conference.** International Hotel, Los Angeles. Saturday-Sunday. Contact: Mathew E. O'Keefe, 402 E. Hadley Street, Whittier.

January 31-February 1—**Uroradiology.** UCLA. Monday-Tuesday.

## FEBRUARY

February 1-March 22—**Isotope Techniques in the Health Sciences.** UCSF. Tuesdays.

February 1-April 19—**Bedside Diagnosis of Cardiac Disease.** USC at Los Angeles County Hospital. Tuesday evenings, 24 hours. \$80.

February 2-4—**Aviation Medicine Seminars.** UCSF at Del Webb's Townhouse, San Francisco. Wednesday-Friday.

February 3-4—**SOUTHERN COUNTIES—Regional Postgraduate Institute presented by California Medical Association** in cooperation with USC School of Medicine. El Mirador Hotel, Palm Springs. Thursday-Friday. \$15. "Cardiovascular Disease, Hematology and Infectious Diseases, Antibiotics." Chairman: Robert M. Zweig, M.D., 3875 Jackson, Arlington.

February 4-5—**New Potentials in Diagnosis and Treatment.** UCSF. Friday-Saturday. 12½ hours. \$40.

February 4-March 11—**Psychiatry in Daily Practice.** UCSF at Mercy Hospital, Redding. Fridays.

February 5-6—**Arthritis: A Symposium for the Medical Practitioner.** USC. Saturday-Sunday. 12 hours. \$25.

February 7—**Medical Aspects of Well Being: Emotional Aspects of Rehabilitation.** UCSF. Monday.

February 7-March 14—**Contra Costa County Heart Association Postgraduate Course for Physicians.** John Muir Hospital, Walnut Creek. Mondays. 12 hours. \$15. Contact: Loyse C. Casebolt, executive director, 1541 East Street, Walnut Creek.

February 9—**Circulatory Shock.** USC at Sheraton-West Hotel, Los Angeles, Wednesday. 8:30 a.m.-4:45 p.m. \$25.

February 10—**Los Angeles Pediatric Society Annual Parmelee Memorial Lecture.** Los Angeles County Medical Association Building, 1925 Wilshire Blvd., Los Angeles. Thursday. 6:30-9:30 p.m. Contact: Paul F. Wehrle, M.D., program chairman, 9209 6th Ave., Inglewood 90305.

February 10-11—**Symposium on Endocrinology.** USC at Statler Hilton Hotel, Los Angeles. Thursday-Friday. 12 hours.

February 10-12—**The Specialties in Pediatric Office Practice.** UCSF. Thursday-Saturday.

February 11-13—**American College of Physicians, Northern California and Nevada Regional Meeting.** Mark Thomas Inn, Monterey. Friday-Sunday. 10 hours. Contact: Roberto F. Escamilla, M.D., Governor, ACP, NCNR, 897 Hyde Street, San Francisco.

February 12—**Surgical Emergencies.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

February 12-13—**Cystic Fibrosis.** UCLA. Saturday-Sunday.

February 12-13—**A Symposium on Hypnosis.** UCSF at Napa State Hospital, Imola. Saturday-Sunday.

February 12-13—**Law-Science-Medicine.** UCSF. Saturday-Sunday.

February 12-13—**The Patient, His Disease and His Family.** USC in Phoenix. Saturday-Sunday. 12 hours. \$25.

February 14-16—**Institute for Metabolic Research Dynamics of Endocrine and Metabolic Disease An-**

**nual Symposium.** Highland Hospital. Monday-Wednesday \$30. Contact: L. W. Kinsell, M.D., director, Institute of Metabolic Research, 2701 14th Ave., Oakland.

February 14-18—**American College of Chest Physicians—Clinical Application of Cardio-Pulmonary Physiology.** Ambassador Hotel, Los Angeles. Monday-Friday. Contact: Alfred Goldman, M.D., program chairman, Suite 906, 9201 Sunset Blvd., Los Angeles 90069.

February 14-18—**Course for Physicians in General Practice.** UCSF at Mt. Zion Hospital, San Francisco. Monday-Friday.

February 16-20—**Controversial Areas in Surgery.** UCLA at Palm Springs. Wednesday-Sunday.

February 18-19—**Pediatric Dermatology.** UCSF. Friday-Saturday.

February 18-20—**American College of Physicians Southern California Regional Meeting.** Biltmore Hotel, Santa Barbara. Friday-Sunday. Contact: W. Philip Corr, M.D., governor, 3660 Arlington Avenue, Riverside 92506.

February 19-20—**Neuropsychiatry in Daily Practice.** UCSF in Salinas. Saturday-Sunday.

February 20-23—**Current Concepts in Chemotherapy.** UCLA at Palm Springs. Sunday-Wednesday.

February 24-25—**Medical-Surgical Gastroenterology Conference.** USC. Thursday-Friday.

February 25—**Annual Sterling Bunnell Memorial Lecture on Reconstructive Surgery.** Lane Hall, Pres. Med. Ctr. Friday. 8:00 p.m. Contact: Donald R. Pratt, M.D., chairman, 516 Sutter Street, San Francisco 94102.

February 25-26—**Workshop on Hand Injuries.** Pres. Med. Ctr. Friday-Saturday. 12 hours. \$75.

February 25-27—**Conference on Mental Retardation for Physicians.** UCSF. Friday-Sunday.

February 27-March 2—**Surgical Applied Anatomy.** LLU. Sunday-Wednesday. 29½ hours. \$100.

## MARCH

March 2-3—**Los Angeles County Heart Association Annual Spring Symposium.** Statler Hilton Hotel, Los Angeles. Wednesday-Thursday. 12 hours. Contact: Professional Symposium Committee, LACHA, 2405 W. Eighth Street, Los Angeles 90057.

March 2-3—**Western Electroencephalography Society Annual Meeting.** Hilton Hotel, San Francisco. Wednesday-Thursday. Contact: Edward E. Shev, M.D., secretary treasurer, 516 Sutter Street, San Francisco.

March 2-4—**American Medical Association Air Pollution Medical Research Conference.** Ambassador Hotel, Los Angeles. Wednesday-Friday. Contact: Air Pollution Medical Research Conference, Department of Environmental Health, AMA, 535 N. Dearborn Street, Chicago, Illinois 60610.

March 3-4—**Symposium on Diabetes.** USC at the Ambassador Hotel, Los Angeles. Thursday-Friday. 14 hours.

March 4-5—**Gynecological Problems for the Non-Gynecologist.** UCSF. Friday-Saturday.

March 4-5—**Operable Heart Disease.** Pres. Med. Ctr. Friday-Saturday. 16 hours. \$35.

March 5-6—**The Knee.** UCLA. Saturday-Sunday.



March 5-6—**Sex Education and the Family Doctor.** UCSF at Herrick Hospital, Berkeley. Saturday-Sunday.

March 9-11—**Conference on Keratoplasty.** Pres. Med. Ctr. Wednesday-Friday, 21 hours. \$125. Contact: Lions Eye Foundation, Pres. Med. Ctr., 2018 Webster Street, San Francisco 94115.

March 9-13—**Diagnostic Radiology.** UCSF. Wednesday-Sunday.

March 10—**Symposium on Obesity.** USC at the Ambassador Hotel, Los Angeles. Thursday. 7 hours.

March 10-14—**Pulmonary Problems.** UCLA. Thursday-Sunday.

March 11-12—**Childrens Hospital Medical Center Annual Postgraduate Seminar and Clifford D. Sweet Lecture.** Childrens Hospital, 51st and Grove Streets, Oakland. Friday-Saturday. 16 hours. \$30 for 4 sessions or \$10 per session. Contact: Miss Inetta Carty, Medical Staff Office. Childrens Hospital Medical Center, Oakland.

March 11-12—**WEST COAST COUNTIES—Regional Postgraduate Institute** presented by California Medical Association in cooperation with UCSF. Ojai Valley Inn, Ojai. Friday-Saturday. \$15. "Indications for Surgical Intervention—The Difficult Decision." Chairman: George J. Wittenstein, M.D., 2235 Castillo, Santa Barbara.

March 12—**Cancer: Childhood and Adult Tumors.** UCSF at Childrens Hospital, San Francisco. Saturday.

March 12—**Obstetrics and Gynecology.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

March 12-13—**Neuropsychiatry in Daily Practice.** UCSF at Agnews State Hospital, San Jose. Saturday-Sunday.

March 13-17—**Alumni Postgraduate Convention, LLU.** March 13-14 (Sunday-Monday)—Refresher Courses. White Memorial Medical Center. March 15-17 (Tuesday-Thursday)—Scientific Assembly. Ambassador Hotel, Los Angeles. Contact: Samuel H. Fritz, M.D., general chairman, 1832 E. Michigan Avenue, Los Angeles 90033.

March 13-April 11—**Medical Centers of Egypt, Jordan, Lebanon, Turkey, Greece and Italy.** Sponsored by USC. 39 hours. \$200.

March 16—**Annual Postgraduate Symposium on Heart Disease.** O'Connor Hospital, San Jose. Wednesday. \$15., incl. lunch. Contact: William G. Allayaud, executive director, Santa Clara County Heart Association, 1961 The Alameda, San Jose 95126.

March 16—**Symposium on Obesity.** USC. Wednesday.

March 19—**Catecholamines and Adrenergic Blocking Agents.** Sponsored by the American College of Cardiology and USC. Ambassador Hotel, Los Angeles. Saturday. Members: \$20., Non-Members: \$25. Contact: Executive Director, ACC, 9650 Rockville Pike, Washington, D.C. 20014.

March 19—**Rheumatic Diseases: Diagnosis and Treatment.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

March 19-20—**California Radiological Society Annual Meeting.** Biltmore Hotel, Los Angeles. Saturday-Sunday. Contact: L. H. Garland, M.D., 450 Sutter Street, San Francisco.

March 20—**American College of Chest Physicians California Chapter Annual Meeting.** Biltmore Hotel, Los Angeles. Sunday. 9:00 a.m.-4:30 p.m. Contact: M. Rosenblatt, M.D., program chairman, County of Los

Angeles Health Department, 220 North Broadway, Los Angeles 90012.

March 20-23—**CALIFORNIA MEDICAL ASSOCIATION 95th Annual Session.** Scientific theme: "CURRENT CONCEPTS IN THERAPY: Coronary Artery Disease. Gastrointestinal Hemorrhage. Renal Failure." Biltmore Hotel, Los Angeles. Sunday-Wednesday. Contact: California Medical Association, 693 Sutter Street, San Francisco 94102.

March 25-27—**Postgraduate Assembly in Anesthesiology.** Sponsored by the Anesthesia Section, Los Angeles County Medical Association. International Hotel, Los Angeles. Friday-Sunday. 12 hours. \$25. Contact: Thomas W. McIntosh, M.D., secretary, Postgraduate Committee, 686 East Union Street, Pasadena.

March 25-27—**Sex Disorders in Clinical Practice.** UCSF. Friday-Sunday.

March 26—**Endocrinology.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

March 29-30—**Southwestern Pediatric Society.** Statler Hilton Hotel, Los Angeles. Tuesday-Wednesday. Contact: Phillip Sturgeon, M.D., 1200 S. Vermont Avenue, Los Angeles 90006.

#### APRIL

April 1—**Fresno County Heart Association Annual Physicians Cardiovascular Symposium.** Hacienda Hotel, Fresno. Friday. \$15. Contact: Roger K. Larson, M.D., chairman, Professional Symposium Committee, FCHA, 1759 Fulton Street, Fresno.

April 1-2—**Contrast Media in Abdominal Disease: A Program for the Practicing Physician.** UCSF. Friday-Saturday.

April 1-2—**Joint Manipulations in Perspective.** UCSF. Friday-Saturday.

April 4-8—**Mental Retardation Institute.** USC. Monday-Friday.

April 5-8—**American Association of Anatomists.** San Francisco Hilton, San Francisco. Tuesday-Friday. Contact: Russell T. Woodburne, executive secretary, The University of Michigan East Medical Bldg., Ann Arbor, Michigan 48104.

April 6-27—**Advanced Funduscopy.** USC. Wednesdays.

April 6-May 11—**Psychiatry in General Practice.** UCSF at Stockton State Hospital, Stockton. Wednesdays.

April 7-June 9—**Ward Walks in Rare Diseases.** USC. Thursdays.

April 12-June 14—**Bedside Cardiology.** USC at St. Vincent's Hospital. Tuesdays.

April 13-15—**The Pacific Regional National Rehabilitation Association Conference.** Sheraton-Palace Hotel, San Francisco. Wednesday-Friday. \$12., including keynote luncheon. Contact: Tak Taketa, chairman, Publicity Committee, 1111 Jackson Street, Rm. 5040, Oakland 94607.

April 13-16—**American Orthopsychiatric Association.** San Francisco Hilton, San Francisco. Wednesday-Saturday. Contact: Marion F. Langer, Ph.D., executive secretary, 1790 Broadway, New York 10019.

April 14-16—**Retinal Detachment Conference.** Lions Eye Bank. Thursday-Saturday. 8 hours. \$100. Contact: Eva del Oro, secretary, Lions Eye Bank, 2018 Webster Street, San Francisco.

April 16—**Sports Injuries.** UCLA. Saturday.

April 16-17—**The Uncertain Quest: The Teen-Ager's World.** UCSF. Saturday-Sunday.

April 21-23—**Endocrinology and Metabolism.** UCSF. Thursday-Saturday.

April 23-24—**Neuropsychiatry for the Non-Psychiatric Physician in General Practice.** UCSF at Sutter Memorial Hospital, Sacramento. Saturday-Sunday.

April 25-27—**Annual Meeting of the Council on Medical Television.** UCSF. Monday-Wednesday. Contact: Irving Merrill, M.D., director, Office of Television Research, UCSF.

April 28-29—**General Surgery.** UCSF. Thursday-Friday.

April 28-29—**Symposium on Hypertension.** USC. Thursday-Friday.

April 29-May 1—**REDWOOD REGIONAL CONFERENCE presented by California Medical Association in cooperation with USC.** Konocti Harbor Inn, Clear Lake. Friday-Sunday. \$15. "Cardiovascular Disease, Endocrinology, Office Techniques in Patient Interviews." Chairman: Lucius L. Button, M.D., 1102 Montgomery Drive, Santa Rosa.

## MAY

May 1-5—**American Society for Microbiology.** Biltmore Statler Hilton Hotel, Los Angeles. Sunday-Thursday. Contact: R. W. Sarber, executive secretary, 115 Huron View Blvd., Ann Arbor, Michigan.

May 5-7—**Ear, Nose, Throat.** UCSF. Thursday-Saturday.

May 5-26—**Neuropsychiatric Management in Daily Practice.** UCSF at Modesto State Hospital, Modesto. Thursdays.

May 6-7—**Obesity.** UCSF. Friday-Saturday.

May 7—**Ventura County General Hospital Annual Staff Seminar.** VCGH. Saturday. 6 hours. No fee. Contact: G. K. Ridge, M.D., VCGH, 3291 Loma Vista Road, Ventura.

May 7-8—**Dynamic Measurements with Radioisotope Techniques for Evaluating Organ Function and Circulation.** UCLA. Saturday-Sunday.

May 12-15—**Hawaii Medical Association Annual Meeting.** Arthritis and Psychiatry. Princess Kaiulani Hotel, Honolulu. Thursday-Sunday. 15 hours. \$35. Contact: Miss Lee McCaslin, executive secretary, 510 S. Bere-tania, Honolulu, Hawaii 96813.

May 13—**The Modern Cardiovascular Practitioner.** UCSF at Redwood Empire Heart Association, Santa Rosa. Friday.

May 13-14—**Convulsive Disorders.** UCSF. Friday-Saturday.

May 13-14—**SAN JOAQUIN VALLEY COUNTIES—Regional Postgraduate Institute presented by California Medical Association in cooperation with UCLA.** Ahwahnee Hotel, Yosemite. Friday-Saturday. \$15. "Cerebral and other Peripheral Vascular Disease, Headache. Chairman: Dale Kirkegaard, M.D., 2432 Calaveras Street, Fresno.

May 14—**Humboldt-Del Norte Medical Society Annual Medical Symposium: "Frontiers in Medicine."** Eureka Inn, Eureka. Saturday. 4 hours. Contact: Stan-wood S. Schmidt, M.D., president, 707 K Street, Eureka.

May 19—**California Heart Association Annual Scientific Session.** Ambassador Hotel, Los Angeles. Thursday. 6 hours. No fee. Contact: Arthur Feinfeld, M.D., CHA, 1370 Mission Street, San Francisco.

May 21—"Clinic Day"—**Diseases of Medical Progress.** Channing House Auditorium, Palo Alto. Saturday. 9:00 a.m. to 3:30 p.m. Contact: R. Hewlett Lee, M.D., Palo Alto Medical Clinic, 300 Homer, Palo Alto.

May 21-22—**Health of the School Child.** UCSF. Saturday-Sunday.

May 23-25—**American Thoracic Society Annual Meeting.** Hilton Hotel, San Francisco. Monday-Wednesday. Contact: James Kieran, M.D., chairman, Medical Sessions Committee, American Thoracic Society, 1790 Broadway, New York, N.Y. 10019.

May 28-June 29—**Medical Centers of Europe.** USC. 50 hours. \$250.

May 20-21—**San Diego Academy of General Practice Annual Postgraduate Symposium** in cooperation with University of Oregon School of Medicine. Vacation Village Hotel, Mission Bay, San Diego. Friday-Saturday. Contact: Orlando P. Johann, M.D., 731 E. Broadway, El Cajon.

## JUNE

June 17—**Attending Staff Association of Olive View Hospital Symposium on Infectious Diseases.** OVH, Olive View. Friday. Contact: Joseph K. Indenbaum, M.D., secretary-treasurer, ASAOVH, Olive View.

June 22-24—**Highlights of Modern Ophthalmology.** Lions Eye Bank. Wednesday-Friday. 8 hours daily. \$75. Contact: Eva del Oro, secretary, Lions Eye Bank, 2018 Webster Street, San Francisco.

June 22-24—**Treatment of Fractures.** USC. Wednesday-Friday.

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## Who Doesn't Follow The Doctor's Orders?

Nearly one-third of all patients apparently fail to follow the orders of their physicians—and, a new study indicates, many physicians fail to realize this.

Results of the study by Milton S. Davis, Ph.D., associate professor of sociology in medicine, Cornell University Medical College, are reported in the Medical News section of the November 1 *Journal of the American Medical Association*.

Obviously, Dr. Davis said, the value of diagnosis and prescription may be severely limited if the patient fails to follow his doctor's orders.

The type of patient least likely to comply:

"An older person; more likely a woman than a man; from a lower, socio-economic level, and probably with a lower level of education," he said.

What does the physician do when he learns that the patient isn't following his advice?

Generally, he first tries further explanation of the need, physicians told Dr. Davis. Then he tries persuasion.

If that doesn't work, the senior physician is more likely to withdraw from the case, an option not always available to younger men working in clinics or on hospital staffs.

Dr. Davis based his report on an analysis of 27 previous studies of patient non-compliance, plus a survey of 132 senior physicians on the faculty of a teaching hospital and 86 junior physicians or senior medical students working in the hospital's outpatient service.

The orders most frequently ignored, Dr. Davis said, are those which require the patient to change his personal habits or behavior—stop smoking, lose weight, get more sleep.

Frequent non-compliance is reported when the physician advises eye and ear examinations, and delays are frequent when surgery is suggested.

In general, Dr. Davis said, advice in the medical area is followed more frequently than that which suggests surgery.

Medical advice which is complex, or which requires the patient to do more than one thing at a time, is less likely to be followed.

Dr. Davis said he has tentatively concluded that an age factor may play a part in non-compliance. Those between ages 46 and 65 seem less likely to comply.

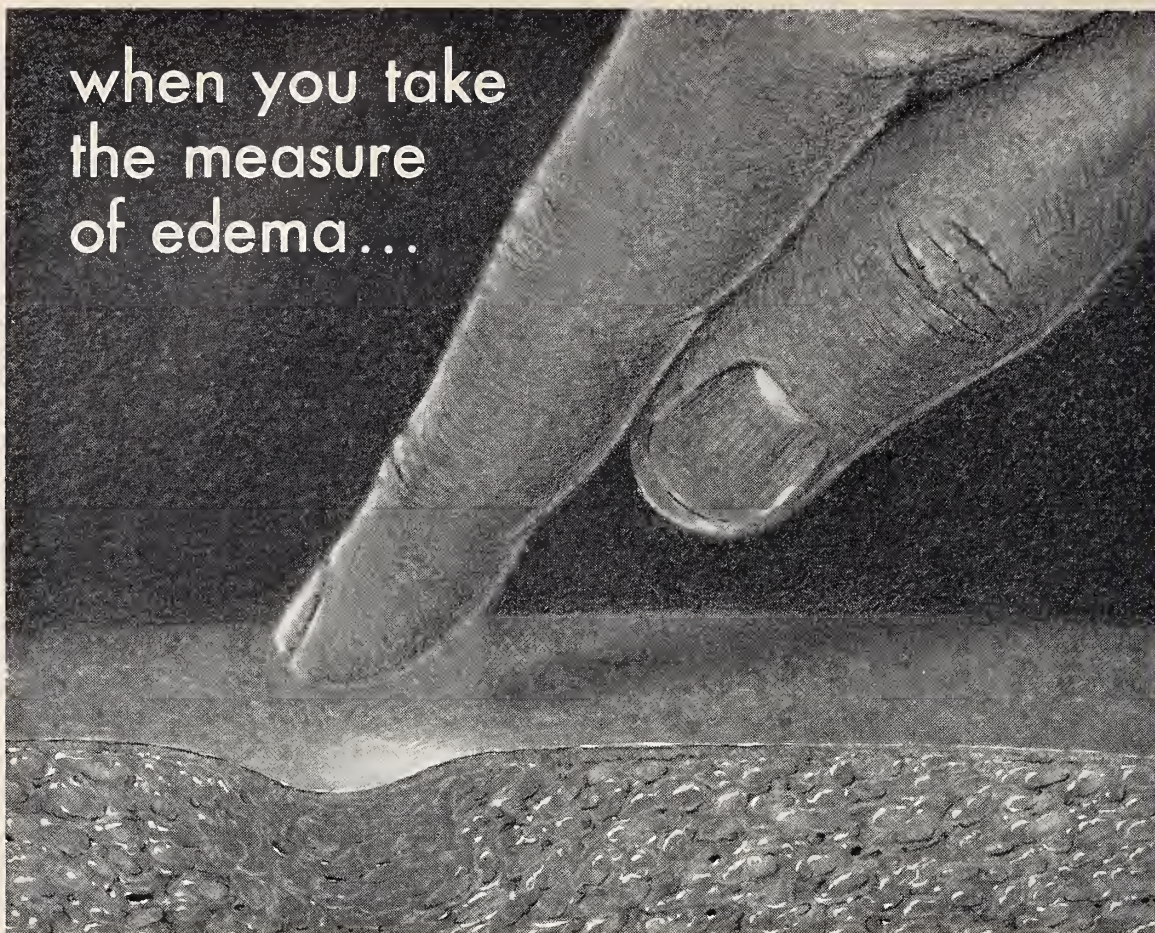
Previous studies indicate, he said, that from 15 to 82 per cent of patients fail to follow directions offered by their physicians. The degree of non-compliance varies with numerous factors, but averages about 35 per cent in all studies.

Yet, 42 per cent of the physicians questioned by Dr. Davis estimated that "almost all" of their patients followed their advice. Another 47 per cent


(Continued on Page 56)



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diarrhea, dizziness, paresthesia, photosensitivity and headache. Insulin requirements may be altered in diabetes.

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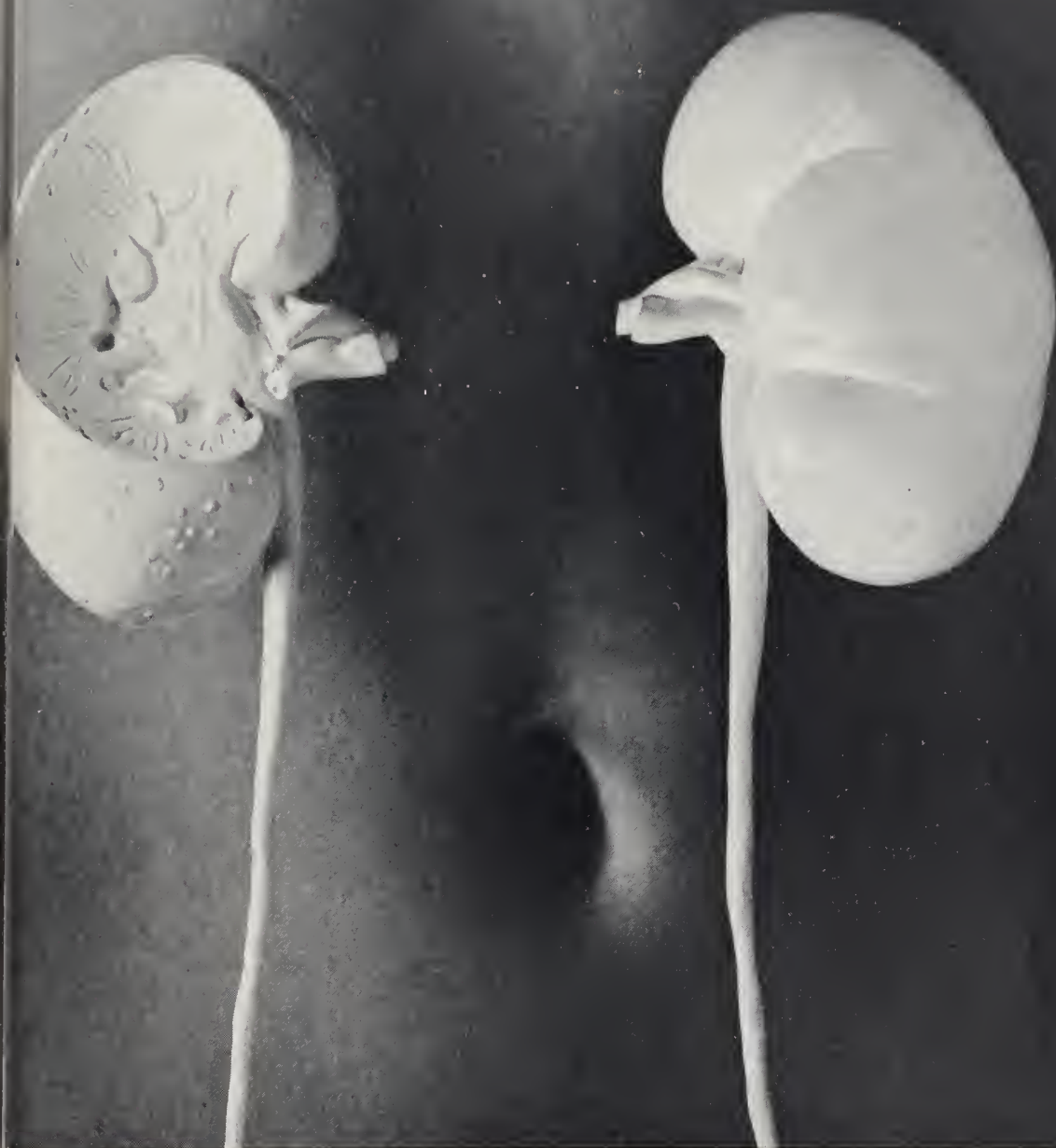
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## Who Doesn't Follow The Doctor's Orders?

(Continued from Page 47)

estimated that three-fourths of their patients do as they are told.

Junior physicians were more accurate than their teachers in estimating the degree to which patients fail to comply. Dr. Davis suggested that this may be due to less certainty among the younger men as to the effectiveness of their advice and to the fact that they may be closer to their patients in the socio-economic scale.

## New Research Facility of AMA Is Dedicated to Study of Basic Life Processes

The laboratories of an important new research facility opened for business with the dedication of the Institute for Biomedical Research of the American Medical Association Education and Research Foundation.

The purpose of the Institute is to provide a privately supported basic research facility of excellence in which the investigator-members may devote their interests to work without any other duties except as they may elect. As such, the Institute is a manifestation of the recognition, interest and support given to basic research by the American physician.

Recognizing that biology is the study of the life processes, and that diseases are aberrations of these processes, the Institute is devoted to the support of fundamental inquiry into the life processes on all basic levels. It does not focus attention on disease-oriented programs except to aid the individual scientist in research. The Institute undertakes no dictated research activities or applied research. A typical area of Institute interest is molecular biology, including experimental ecology, biochemical genetics, and antibody synthesis.

Institute Director is Roy E. Ritts, Jr., M.D. Investigators appointed to the Institute as of November 1 are Howard A. Schneider, Ph.D.; Clyde R. Goodheart, M.D.; Dan W. Urry, Ph.D.; and John J. Cebra, Ph.D. George R. Collins is director of the Institute's Animal Research Facility.

Dr. Schneider will continue to work with a disease resistance factor, which he calls pacifarin, found as a contaminant in certain foods. Twenty years of investigation have convinced Dr. Schneider that the pacifarin compounds are in reality a group of previously unknown entities that may be among the most potent disease inhibitors ever found.

Even a microscopic amount of a pacifarin extracted from wheat or dried egg white will protect mice against infection by mouse typhoid bacteria. Although mouse typhoid is the only disease for which a pacifarin has been found, Dr. Schneider believes that there are other pacifarins capable of preventing other diseases.





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1. Conant, R. G.: Reduction of industrial time-loss: treatment with carisoprodol compound in musculoskeletal disorders. *Industr. Med. Surg.* 33:25, Jan. 1964.

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**Indications:** 'Soma' Compound and 'Soma' Compound with Codeine are useful for relief of pain and stiffness in traumatic, rheumatic and other conditions affecting muscles and joints. **Contraindications:** Allergic or idiosyncratic reactions to carisoprodol, phenacetin, or codeine phosphate. **Precautions:** *Phenacetin*—With long-term use, give cautiously to patients with anemia and cardiac, pulmonary, renal or hepatic disease. May damage the kidneys when used in large amounts or for long periods. *Caffeine*—Not recommended for persons extremely sensitive to its CNS stimulating action. *Codeine phosphate*—Use with caution in addiction-prone individuals. *Carisoprodol*—Like other central nervous system depressants, should be used with caution in patients with known propensity for taking excessive quantities of drugs and in patients with known sensitivity to compounds of similar chemical structure, e.g. meprobamate. **Side effects:** Drowsiness, lightheadedness, dizziness, and gastric complaints have been reported infrequently for either or both of these preparations. *Phenacetin*—Side effects are extremely rare with short-term use of recommended doses. Prolonged ingestion of overdoses may produce dyspnea, cyanosis, hemolytic anemia, skin rash, anorexia, subnormal temperature, insomnia, headache, mental disturbances, and tolerance. *Caffeine*—Side effects are almost always the result of overdosage. Average doses may rarely cause nausea, nervousness, insomnia, and diuresis. Excessive dosage may produce, in addition, restlessness, nervousness, tolerance, tinnitus, tremors, scintillating scotomata, tachycardia, and cardiac arrhythmias. *Codeine phosphate*—Possible side effects are nausea, vomiting, constipation, and miosis. *Carisoprodol*—The only side effect reported with any frequency is sleepiness, usually on higher than recommended doses. An occasional patient may not tolerate carisoprodol because of an individual reaction, such as a sensation of weakness. Other rarely observed reactions have included dizziness, ataxia, tremor, agitation, irritability, headache, increase in eosinophil count, flushing of face, and gastrointestinal symptoms. One instance each of pancytopenia and leukopenia, occurring when carisoprodol was administered with other drugs, has been reported, as has an instance of fixed drug eruption with carisoprodol and subsequent cross-reaction to meprobamate. Rare allergic reactions, usually mild, have included one case each of anaphylactoid reaction with mild shock and angioneurotic edema with respiratory difficulty, both reversed with appropriate therapy. In cases of allergic or hypersensitivity reaction, carisoprodol should be discontinued and appropriate therapy initiated. Suicidal attempts may produce coma and/or mild shock and respiratory depression. **Dosage:** Usual adult dosage of 'Soma' Compound or 'Soma' Compound with Codeine is one or two tablets three times daily and at bedtime. Supplied: 'Soma' Compound, orange tablets, each containing carisoprodol 200 mg., phenacetin 160 mg., and caffeine 32 mg. 'Soma' Compound with Codeine, white capsule-shaped tablets, each containing carisoprodol 200 mg., phenacetin 160 mg., caffeine 32 mg., and codeine phosphate 16 mg. Narcotic order form required. *Before prescribing, consult package circular.*

CSO-4512

## REFERENCES AND REVIEWS

**NEUTRALIZATION OF LONG-ACTING THYROID STIMULATOR BY ANTIBODIES TO EUTHYROID HUMAN SERUM**—D. D. Adams and A. Sharard (University of Otago Medical School, Dunedin, New Zealand). *Aust. Ann. Med.* 14: 192-194 (No. 3) 1965.

Antiserum to unfractionated euthyroid human serum, prepared in the goat, neutralized the thyroid-stimulating activity of a highly potent long-acting thyroid stimulator (LATS) preparation. Absorption tests with gamma globulin and with albumin showed that the neutralizing antibodies were anti-gamma globulins. These findings, together with previous observations, make it probable that LATS is itself a gamma globulin.

\* \* \*

**ROLE OF CITRATE IN ABNORMAL COPPER METABOLISM**—R. Nath and S. K. Srivastava (Indiana University School of Medicine, Indianapolis). *Metabolism*, 14: 1237 (Dec.) 1965.

Serum citric acid and ceruloplasmin activity were determined in one case of Wilson's disease and another of acute copper poisoning in man. Elevation of citric acid and loss of ceruloplasmin activity were noted in both cases. In the case of copper poisoning, citrate and ceruloplasmin content of serum returned to normal levels after five days of dimercaprol (BAL) treatment.

\* \* \*

**DISTRIBUTION OF JUXTAGLOMERULAR GRANULES**—E. C. Frieburg (3395 Scranton Rd., Cleveland). *Arch. Path.*, 80:621 (Dec.) 1965.

Adult mice were kept on a diet largely free of sodium

chloride for 30 days. Histological examination of the juxtaglomerular granules revealed a significant increase in the juxtaglomerular index affecting the outer and middle zones of the renal cortex. The juxtaglomerular index of the inner zone remained unaltered. The granulated cells were observed to be largely confined to the walls of the afferent arterioles, sometimes extending for a considerable distance along the length of an arteriole.

\* \* \*

**ISOIMMUNITY WITHOUT DEMONSTRABLE ANTIBODIES**—J. J. van Loghem et al. (Central Laboratory, NRC Blood Transfusion Service, POB 200, Amsterdam, Netherlands). *Transfusion*, 5:525 (Nov.-Dec.) 1965.

Survival studies performed in human subjects using donor red cells labeled with radioactive chromium 51 showed that in the absence of demonstrable humoral isoantibodies isoimmunity can still exist. Three groups of persons were investigated: (1) patients with hypogammaglobulinemia, (2) donors with blood group A lacking anti-B, and (3) patients with hemolytic transfusion reactions.

\* \* \*

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## Artificial Heart Valves Questioned

Two prominent surgeons have called for a hard second look at the use of artificial heart valves.

While acknowledging the value of artificial valves in extreme cases, they say that the valves have been overused.

Sir Russell Brock, president of the Royal College of Surgeons, advocates more use of heart valves transplanted from cadavers. It may even be possible to transplant heart valves from other animals, he suggested.

Charles P. Bailey, M.D., director of thoracic and cardiovascular surgery at St. Barnabas Hospital, New York City, has led research in repairing existing heart valves with other tissue from the patient's body. This may prove more successful than artificial valves, he said.

The two surgeons' comments appear in the Medical News section of the December 27 *Journal of the American Medical Association*. They spoke at a symposium on rheumatic and coronary heart disease sponsored by St. Barnabas Hospital.

Artificial heart valves haven't been in use long enough to evaluate their long-term survival rate, Dr. Bailey said. Nevertheless, failure rates as high as 37 per cent within 12 months after implantation have been reported.

Valve-repair techniques at least equal the survival rate of artificial heart valves, and should be expected to surpass it, Dr. Bailey said.

"Obviously, when a patient has no future without an operation, valve (removal) is not only justifiable, but can be a brilliant, worthy and highly commendable form of treatment," Sir Russell said. "There is, however, much evidence that the limitations of valve (removal) and replacement are often totally ignored."

Sir Russell's main objection to the artificial valve is that it represents too radical a departure from the natural valve's shape. He questions whether an artificial valve will be long tolerated by the body.

Improvements in cadaver-valve transplantation techniques have produced excellent results with low death rates, he said.

At Guy's Hospital in London, where Sir Russell is director of cardiology, the aortic valves of more than 100 patients have been replaced with valves from cadavers. The earliest of these patients has now survived 3½ years.

While agreeing that the artificial valve has limited use, Dr. Bailey differed somewhat on alternative procedures. He favors reconstructing the original valve with other tissue from the patient's body.

There have been complications in replacing sections of artery with sections from cadavers, and these complications probably apply to the more difficult task of heart-valve replacement, he said.

In addition, it is difficult to obtain an adequate

(Continued on Page 16)



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References: 1. Handelman, Cathryn C.: Early management of acne, *Pediat. Clin. North America* 8:265, Feb., 1961. 2. McLean, I. E. D.; Graham, K. T., and East, M. O.: The treatment of acne; a trial of "pHisoHex," *Practitioner* 189: 82, July, 1962. 3. Hodges, F. T.: Therapeutic applications of an antiseptic detergent, *GP* 14:86, Nov., 1956. 4. Wexler, Louis: Treatment of acne vulgaris, *Clin. Med.* 70:404, Feb., 1963.

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## Artificial Heart Valves Questioned

(Continued from Page 13)

supply of cadaver heart valves, Dr. Bailey said.

Sir Russell agreed that supplying a variety of heart valve sizes from cadavers is difficult.

"The solution may lie in the use of heterograft valves (from other animals), and we should not turn lightly from developing their wide use unless it is shown that they are not satisfactory on immunological grounds," he said.

With further experience, the need for artificial heart valves may be reduced to only occasional aged and terminally ill younger patients, Dr. Bailey said.

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valves in recent years should not blind the surgeon to the fact that it is, in reality, a great human experiment, Sir Russell warned.

"It can be argued very reasonably that it is an investigation that has to be made, an experiment that has to be tried. This is entirely justifiable if we remember that it is an experiment, a deliberate, widespread human experiment," he said.

## Running or Fright: Which Comes First?

One of the most significant findings from the abortive attempt to orbit Gemini 6, December 12, so that it could rendezvous with Gemini 7 concerns the "run and fright" theory.

The January 3 issue of *The AMA News*, published by the American Medical Association, tells of new findings that the attempted launch contributed to the theory.

The situation was this:

Command Pilot Walter M. Schirra had four-tenths of a second to decide whether he should eject himself and pilot Thomas P. Stafford from the vehicle. He decided not to eject.

The rocket engines fired for 1.2 seconds. Had they gone to 1.6, ejection would have been the only way for the two pilots to save themselves. Schirra had to decide whether so much thrust had already built up that ejection was the only way out.

The chief physician for the astronauts, Charles A. Berry, M.D., noted that at the most critical point in the unsuccessful launch, "Schirra was remarkably calm and cool. It wasn't until one minute later, after he had made the right decision and everything looked as if it would be okay, that his pulse rate started going up."

"The only way I can explain that the rise occurred after the emergency," Dr. Berry said, "is on the basis that Schirra literally didn't have time to get scared during the emergency itself. He just acted, and what he did, of course, was the very right thing."

The physician said that the sequence of stimuli seems to be as follows: first there is the stimulus that tells people they are in danger. If, as in the case of astronauts, they have been trained to anticipate such emergencies, the vital signs do not reflect the perception of danger until action has already been taken. After such action, the psychological response—the fright—comes along.

Dr. Berry was asked whether this seemed to be a confirmation of the theory that fear follows action, or "you get scared because you run."

He said he agrees, provided the theory is examined from the point of view that in this case, the action was not "running," but another kind of decision, and the "fright" was recognition that a true emergency had occurred.



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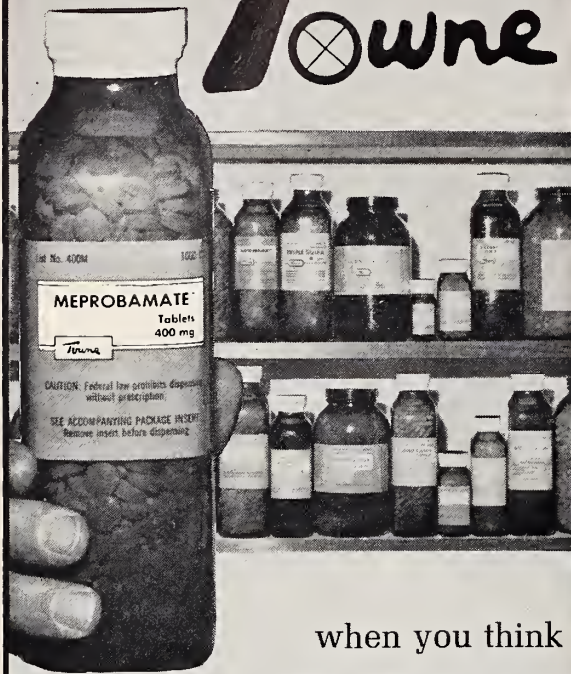
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## Eye Infections from Puppies and Kittens

The protection of children's eyes is another good reason for de-worming puppies and kittens, suggests an article in the December 27 *Journal of the American Medical Association*.

The report tells of a six-year-old girl who never went near dogs or cats, but nonetheless suffered blurred vision and inflammation in one eye for more than a year. At some earlier time, she apparently had swallowed dirt infested with the eggs of *Toxocara canis*, the common dog roundworm.

The larva probably got into the girl's bloodstream, and was carried to the peripheral retina area of her eye. It lived on, healthy and vigorous.

As the report points out, kittens and puppies, not mature dogs and cats, are more likely to spread such infections to people of all ages. Adult cats and dogs are less likely to transmit the disease because previous infections may have established immunity to reinfection and recycling of the larvae.

A tragic part of the story is that the girl died about a year later, of causes unrelated to the eye condition. During that year, however, three physicians at the University of California's San Francisco Medical Center were able to follow the case closely.

As a *Journal* editorial notes, their report is of considerable importance because of the unusual location of the larva, the opportunity to follow the case for such a time, and because this is but the second reported *T. canis* infection of the peripheral retina area.

Such infections may be fairly common, however. "In a recent survey of the types of uveitis (infections of the colored portion of the eye) it was found that 16 per cent of cases suffered from an inflammation similar to the one reported," said the *Journal* editorial.

Of these, about 25 per cent (4 per cent of the total) had an inflammation in only one eye. Larva infections seldom affect both eyes.

"If this 4 per cent all had ocular nematodiasis (eye infections from worms), the disease must be fairly common in this country," the editorial said.

"How is the public to be informed about the need for de-worming young puppies and kittens, so they do not shed ova which can be ingested and lead to human disease?" asked the editorial.

"Too little publicity has been given to the problem by health authorities. Parents are largely unaware of the danger created by infected puppies and kittens in a neighborhood. Veterinarians should be in the vanguard in the dissemination of information about the proper care of young animals," the editorial said.

Authors of the *Journal* article are Michael J.

(Continued on Page 30)



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## Eye Infections from Puppies and Kittens

(Continued from Page 18)

Hogan, M.D., Samuel J. Kimura, M.D., and William H. Spencer, M.D., all of the Francis I. Proctor Foundation for Research in Ophthalmology and the Department of Ophthalmology, University of California, San Francisco Medical Center.

## Ulcer Treatment Has Limited Value

Gastric freezing failed as a treatment for duodenal ulcers in more than nine of every 10 cases studied, four Minnesota physicians report in the January 10 *Journal of the American Medical Association*.

An 18-month follow-up of 173 cases indicates that gastric freezing has limited value in treatment of chronic duodenal ulcer, the doctors said.

In 92.5 per cent of these cases, patients had a return of symptoms or underwent corrective surgery within 18 months after their first gastric freeze procedure. Forty-two of these patients underwent a second freeze, but all had a return of symptoms.

Although freezing often fails to cure the ulcer, it does have remarkable effects on patients: it improves their emotional state.

"We have been impressed with the intense desire of many of our patients to be improved by this form of therapy, which is more vigorous than any they have previously experienced," the authors said.

It appears that "a dramatic therapeutic episode," such as gastric freezing, can improve emotional state without actually improving the physiological aspects of the disease, the physicians said. In some cases, painful symptoms disappeared, even though ulcer-causing secretions of hydrochloric acid remained high.

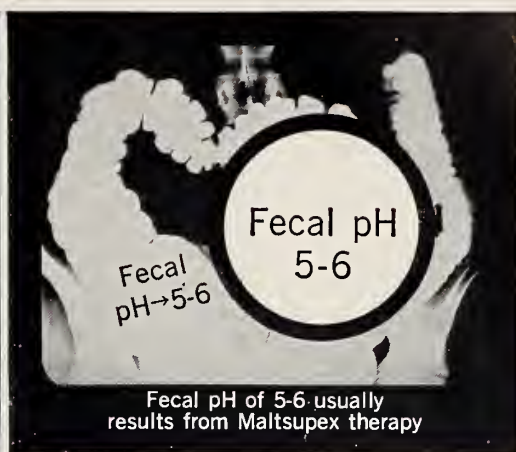
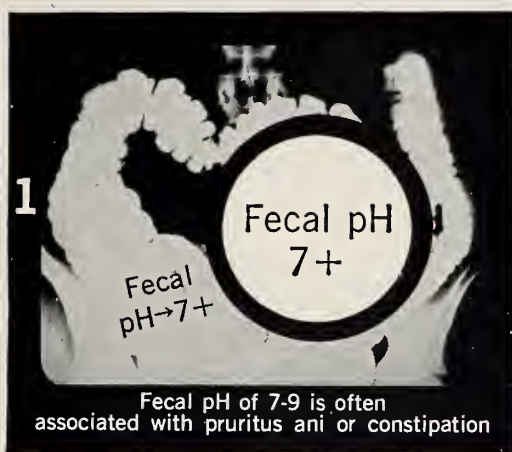
This loss of pain response, however, could be a "prelude to catastrophe," such as a perforation of stomach wall or intestine, the authors said.

Freezing actually does reduce the secretion of acid and pepsin in the stomach, but within six to eight weeks these secretions are as high or higher than pre-freeze levels.

Thus, the authors conclude that carefully performed gastric freezing is a safe procedure for temporarily reducing acid and pepsin secretions for up to eight weeks. When compared to more conservative medical treatment, however, gastric freezing has no better record than earlier ulcer-treatment methods, the authors said.

The authors are Claude R. Hitchcock, M.D., Ph.D., Ernest Ruiz, M.D., R. Duncan Sutherland, M.D., and James E. Bitter, M.D., of the University of Minnesota Medical School and Hennepin County General Hospital, Minneapolis.





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# BOOKS RECEIVED

*Books received by CALIFORNIA MEDICINE are acknowledged in this column. Selections will be made for more extensive review in the interest of readers as space permits.*

**ACTING OUT—Theoretical and Clinical Aspects**—Edited by Lawrence Edwin Abt, Ph.D., and Stuart L. Weissman, Ph.D. Grune & Stratton, Inc., New York, 1965. 336 pages, \$11.50.

**ADVANCES IN BLOOD GROUPING II**—Alexander S. Wiener, M.D., F.A.C.P., Senior Bacteriologist (Serology) to the Office of the Chief Medical Examiner of New York City, Adjunct Associate Professor of the Department of Forensic Medicine of the New York University Medical School, and Attending Immunohematologist to the Jewish and Adelpi Hospitals of Brooklyn, N.Y. With a section by Maurice Shapiro, M.B., B.Ch., F.C.Path., Director, The South African Blood Transfusion Service; Honorary Lecturer in Immunohaematology, University of the Witwatersrand, Johannesburg, South Africa. Grune & Stratton, Inc., New York, 1965. 454 pages, \$12.50.

**ADVANCES IN OXYTOCIN RESEARCH**—Proceedings of a Symposium Held on 1st May 1964, Under the Auspices of the Blair-Bell Research Society at the Royal College of Obstetricians and Gynaecologists, Sussex Place, Regent's Park, London, England; edited by J. H. M. Pinkerton. Pergamon Press, Inc. (Symposium Publications Division), 44-01 21st St., Long Island City, N.Y. 11101, 1965. 150 pages, \$10.00.

**A CURRENT TECHNIQUE OF AORTOILIAC AND FEMOROPOPLITEAL ENDARTERECTOMY FOR OB-LITERATIVE ATHEROSCLEROSIS**—Jack A. Cannon, M.D., Department of Surgery, School of Medicine, University of California, Center for Health Sciences, Los Angeles, California. Charles C Thomas, Publisher, Springfield, Ill., 1965. 54 pages, \$4.75.

**DIAGNOSIS AND THERAPY OF THE GLAUCOMAS—Second Edition**—Bernard Becker, M.D., Professor and Head of the Department of Ophthalmology, Washington University School of Medicine, St. Louis, Mo.; and Robert N. Shaffer, M.D., F.A.C.S., Clinical Professor of Ophthalmology, University of California School of Medicine, San Francisco, Calif. The C. V. Mosby Company, St. Louis, Mo., 1965. 443 pages, \$18.50.

**ELECTROLYTES AND CARDIOVASCULAR DISEASES—Physiology, Pathology, Therapy**—Vol. I, Fundamental Aspects, edited by Eors Bajusz, University of Montreal (Canada). The Williams & Wilkins Company, Baltimore, 1965. 412 pages, \$16.00.

**THE MEDICAL ANNUAL—A Year Book of Treatment and Practitioners' Index**—Sir Ronald Bodley Scott, K.C.V.O., M.A., D.M., F.R.C.P., and R. Milnes Walker, C.B.E., M.S.(Lond.), F.R.C.S., Editors. (Eighty-third Year—1965.) Distributed in the United States, exclusively,

by The Williams & Wilkins Co., Baltimore, Md., 1965. 554 pages, \$10.00.

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REVIEW ARTICLE

# Ambulatory Treatment of the Psychotic Crisis

MORTON R. WEINSTEIN, M.D., *San Francisco*

■ *Current efforts to improve the community-based care of psychiatric patients often include attempts to encourage the ambulatory treatment of acute psychosis by non-psychiatrists. New therapies and revisions of older methods now allow this to be done with many patients for whom, 15 years ago, state hospitalization would have been the first step in treatment, and often the last.*

*Many techniques applicable to the ambulatory treatment of acute psychotic crises can be used effectively by non-psychiatrists. This review describes ambulatory treatment programs for the more commonly encountered acute psychoses. It emphasizes methods which have only recently become available and those which can be used effectively and safely by the non-specialist. With the skillfully combined use of pharmacotherapy, environmental modification, office psychotherapy, legal aids and community resources, the interested nonpsychiatrist can undertake the ambulatory treatment of many psychotic crises.*

ALL AMERICAN PHYSICIANS are witnesses and many are participants in a quiet revolution materially affecting the hundreds of thousands who have had or are destined to have an acute psychotic episode. This revolution, like all major departures in science and in politics, draws its strength from several sources and can be traced to many beginnings. In its background, however, certain events stand out because they summarize and symbolize the longer, slower changes which

preceded them. One such event was the address by Dr. Harry Solomon, then president of the American Psychiatric Association, to that Association's annual convention in 1958, in which he made the extraordinarily far-reaching and influential observation that "our mental hospitals today are bankrupt beyond remedy. I therefore believe that our large mental hospitals should be liquidated as rapidly as can be done in an orderly and progressive fashion."<sup>20</sup> This statement came a few years after Delay and coworkers<sup>9</sup> had introduced chlorpromazine in the treatment of psychoses, and shortly after Loomer, Saunders and

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Kline<sup>21</sup> had reported that the monamine oxidase inhibitor iproniazid was of value in the treatment of depressions.

Other milestones in this medical and social revolution were the passage of the Short Doyle Act for Community Mental Health Services in California in 1957<sup>28</sup> and President Kennedy's Special Message to Congress on Mental Illness and Mental Retardation of February 1963.<sup>18</sup> Finally, the publication in 1961 of Caplan's *Principles of Preventive Psychiatry*<sup>6</sup> is a landmark in the development of programs for effective local treatment of psychiatric illness.

Since the mid-1950's, then, psychopharmacological agents have provided physicians with effective alternatives in the treatment of psychotic illnesses where before hospitalization had dominated the bleak therapeutic landscape. Coincident with and probably in part stimulated by the development of effective drug therapies, there have been energetic attempts to revise and modify standard psychotherapeutic techniques to increase their applicability to psychotic disorders and their usefulness to non-psychoanalysts. Linking each of these innovations, and making them available to large numbers of physicians, post-doctoral psychiatric education has reached and maintained a high level of activity: There are now more postgraduate courses in psychiatry and more students in postgraduate psychiatric training courses than in those of any other specialty.<sup>8</sup>

These are some of the more significant roots of the contemporary revolution in the treatment of ambulatory psychotic patients. In the sections to follow, the application of these techniques to acutely psychotic patients will be considered in detail.

### What Is Acute Psychotic Crisis?

An acute psychotic crisis is a period of rapid behavioral and subjective change characterized by increasing utilization of private or idiosyncratic symbol systems. It implies the more or less sudden development of a significant disparity between the patient's own criteria for causality, and the criteria held by most members of his own cultural group. His departure from conventional modes of estimating causality produces behavioral changes such as poor judgment, apparent lack of concern for conventional social and moral codes, deterioration of conventionalized personal habits, distractibility, perplexity, elevation or depression in mood

or an apparent desynchrony of mood and ideation. A common, probably universal, feature of the acute psychotic crisis is the abandonment of group conventions about logic and symbol manipulation, and the adoption of idiosyncratic logic systems, resulting in disturbance of all aspects of behavior which depend for their effectiveness and acceptability upon sharing most of the symbols and the logic of one's group.

Acute psychotic episodes can be grouped as follows:

- I. *Acute mood disorders*—(a) Acute manic psychoses; (b) acute depressive psychoses.
- II. *Acute schizophrenic episodes*—(a) Characterized by withdrawal and detachment; (b) characterized by perplexity and disorganization; (c) characterized by hallucinations and/or delusions; (d) characterized by excitement and overactivity.
- III. *Acute disorders of perception (acute brain syndromes)*—(a) Following physical trauma; (b) toxic and withdrawal states; (c) associated with metabolic, pulmonary or cardiovascular disturbances; (d) degenerative and abiotrophic.

Acute disorders of perception associated with organic central nervous system damage form a special category of acute psychotic crises. In many instances an etiological diagnosis can be made and specific corrective measures undertaken. However, when treatment based on etiology is not possible, or when acutely disturbed behavior must be managed before treatment based on etiology can have an effect, many of the techniques applicable to the treatment of acute disorders of mood and acute schizophrenic episodes can be utilized advantageously in the emergency management of acute disorders of perception. Because the acute disorders of perception raise so many special questions with regard to diagnosis and specific therapy, they will not be considered further in this review.

### Ambulatory Treatment of Acute Mood Disorders

*Acute Manic Psychoses*—When he contemplates ambulatory treatment of the patient with sudden and severe depression or elevation of mood, the physician's attention and judgment must be focused from the start on the possibility that the patient's seriously defective judgment and



his disturbed mood may lead to self-destructive, socially disruptive or personally embarrassing actions. That is, the physician must decide if the potential for suicide in the depressed patient, or for grandiose failures in judgment in the manic patient, can be prevented with sufficient speed and certainty to justify the risks of ambulatory treatment.

In almost every instance of manic behavior the accelerated and disorganized social and business activities which usually characterize such states can be controlled by means of moderate to large doses of phenothiazine agents such as chlorpromazine (Thorazine®), 200 to 2,000 mg per day in divided doses, or perphenazine (Trilafon®), 48 to 128 mg per day in divided doses. Adequate behavioral control can usually be reached within two weeks by progressively increasing the phenothiazine dosage until a satisfactory reduction in grandiose thinking and manic behavior is achieved. At higher dose ranges, antiparkinson agents should be given concurrently to prevent extrapyramidal symptoms.

Success or failure with such treatment for the ambulatory patient really hinges less on the medications, which are almost *always* effective when properly used, than it does on the availability, in the patient's personal environment, of the supports and protections necessary for ambulatory therapy. Much, therefore, depends on the ability of the physician to estimate and mobilize such support and protection. Are there friends or family members whose positive feelings about the patient have not yet been obliterated by exposure to his grandiosity? Can they be encouraged and trained by the physician to be his collaborators; to encourage the patient to take his medication as prescribed, to discourage his over-involvement in unwise ventures and schemes, to restore and maintain reasonable sleeping and eating patterns and normal living routines? They can be taught that the manic episode will in most instances be relatively brief, and that it will be followed by a return to normal behavior. They can be helped to appreciate the early evidence of a worsening state, and the importance of communicating such observations to the physician. Above all, the physician can help the collaborating friend or relative to understand that the buffeting the manic patient gives those around him will soon cease, and in fact, is likely to cease sooner if it can be tolerated without vengeance, abandonment or retaliation.

A treatment program otherwise adequate for the ambulatory management of an acute manic crisis can founder because manic patients are extremely wearing to those around them. Broadening the base of responsibility and contact to relieve the pressure on relatives or friends can sometimes be accomplished through the skillful use of helping agencies such as visiting nurse services and day treatment centers, or employing temporary paid companions. The problem of ensuring correct drug intake can be partially assumed in many communities by the visiting nurse service. An informed family attorney can share the important task of maintaining watchfulness and control over the manic patient's tendency to engage in grandiose and unwise business dealings. During the ambulatory treatment of a manic episode in a wife and mother, assistance from the homemaker services available in many areas gives support to the patient and minimizes domestic disruption and the impact of the illness on husband and children.

*Acute Depressive Psychoses*—Sudden depressions, severe enough to be considered psychotic, usually occur in middle and late adult life in people of two personality types: (1) the labile, moody, dramatic person who may have a series of severe depressions, either alone or interspersed among periods of manic behavior; (2) the person who tends to be highly organized, conscientious, duty-bound and careful.

Psychotic depressions in the second kind of patient usually occur in the fifth or sixth decade, and tend to be characterized by bodily preoccupation, severe agitation and delusions of worthlessness. Paranoid thought disorders with delusions of persecution and ideas of reference quite like those described by patients with paranoid schizophrenia can occur in any psychotic depressive episode. Initially or for their entirety psychotic depressive crises can be manifested chiefly by somatic preoccupations or delusions about the body. Furthermore, such somatic concerns can occur in the absence of patently depressed mood. Therefore, the non-psychiatrist must be especially alert to such cases, since the patients often make their initial medical contact with the internist, general practitioner, or surgeon and not with the psychiatrist.

The suicide risk must be estimated by any physician contemplating the ambulatory treatment of any patient thought to be significantly depressed. No amount of experience with depressed patients can justify an unequivocal statement that a par-



ticular depressed patient is not a danger to himself; we are limited to making statements of *probability* about the danger of a suicide attempt, using a relativistic frame of reference in which the risk of self-destructive behavior is weighed, as carefully as possible, against the over-protectiveness, disruption of life patterns and social and economic expense of treatment in hospital. Fortunately, the majority of patients about to make a suicide attempt have contact with a physician before doing so.<sup>23,24</sup> Physicians thus have opportunity in most instances to weigh the danger of a self-destructive act. What has prevented greater improvement in our suicide prevention efforts lies more in the realm of not asking than in not having the opportunity to ask.

A history of previous suicide attempts, however "gestural" they may seem; acknowledgment of current thinking about suicide, especially if particular devices and methods are being considered; expressions of pervasive and unyielding hopelessness about the future; a history of suicide or suspicious sudden deaths in family members; evidence that the patient has begun to "get his affairs in order"; and observable improvement in mood independent of effective treatment or improvement in the patient's life situation—all these are useful measures of the suicide risk. The presence of several of these features indicates a degree of suicide risk incompatible with ambulatory treatment, and should thus lead the physician to encourage the patient toward voluntary entry into a psychiatric hospital. Should such indicators of risk be noted, and should the patient decline to enter a hospital voluntarily, the physician is obligated to communicate his estimate of risk to a responsible family member and encourage that person to petition the appropriate court in his jurisdiction to arrange psychiatric examination for the patient, and, if indicated, commitment to hospital.

In communities where psychiatric consultation is available, either privately or at public clinics offering such services, the non-psychiatrist may wish to request a psychiatrist's opinion about the suicide risk. While individual psychiatrists and psychiatric clinics are often unable to offer *treatment time* soon enough to meet the needs of the acutely depressed patient, they are often able to provide the kind of brief *evaluative* service which can help the non-psychiatrist to decide whether to undertake treatment of such a patient himself.

If the estimate of risk in a depressive crisis is

such that ambulatory treatment seems justified, the non-psychiatrist now has at his disposal a relatively new group of effective agents. Antidepressant drugs, properly used, can ameliorate depressive symptoms to a clinically useful degree in about 75 per cent of cases.<sup>2,7</sup> Curiously, they seem less effective in milder, non-psychotic depressions. Two classes of antidepressant drugs are available. One group, the monamine oxidase inhibitors, is represented by nialamide (Niamid®), phenelzine (Nardil®), isocarboxazid (Marplan®), and others. These agents, while useful, sometimes produce troublesome and, rarely, dangerous side effects.<sup>15</sup> Safe and effective use of them requires more experience of the physician and greater frequency of contact with the patient than is the case with the other class of antidepressants, the iminodibenzyl derivatives such as imipramine (Tofranil®), amitriptyline (Elavil®), desipramine (Pertofrane®), and nortriptyline (Aventyl®).

It is wisest for the non-psychiatrist interested in developing skill in the drug therapy of severe depressions to familiarize himself thoroughly with one or two members of the iminodibenzyl group. Generally speaking, it takes one to three weeks to ascertain the ultimate effectiveness of these drugs. In a physically well, intellectually intact patient of normal size a starting dose of 25 to 50 mg per day of one of these compounds would be appropriate. Over a one-to-three-week period a stepwise increase to a maximum of 50 mg three or four times a day is warranted unless significant improvement occurs earlier, at which point the dose should be maintained unchanged for four to six weeks. Should the remission continue, a gradual reduction to a maintenance dose of 50 to 100 mg per day should then be attempted and this dose continued for three to six months before cautious attempt at further reduction.

Concurrent use of the iminodibenzyl and monamine oxidase inhibitor drugs has produced several severe and a few fatal toxic reactions.<sup>2,4,29</sup> Before prescribing an antidepressant drug, therefore, the physician must be certain that the patient has not been taking any drug of the other class. Should the patient already be using any antidepressant drug the physician must continue to use antidepressants of the same class or he must ensure an interval of at least one week free of all antidepressant medication before instituting treatment with a representative of the other group.

Psychiatrists and non-psychiatrists alike must



bear in mind that many patients who do not respond to antidepressant drugs or who respond to them inadequately or too slowly can look forward to rapid, perhaps lifesaving improvement with electroconvulsive treatment. In some communities, clinics or psychiatrists in private practice have established programs for administering electroconvulsive therapy to outpatients; the availability of such a service may make it possible for the non-specialist to have an active and important role in the treatment of severe acute depressions, collaborating with the psychiatrist or psychiatric clinic during a course of ambulatory electroshock therapy.

The severely depressed patient is rarely a proper subject for analytically oriented psychotherapy. However, with remission from an acute depressive crisis, psychotherapy may be indicated for those patients whose depressive episodes appear to have been exacerbations of preexisting neurosis, or the result of maladaptive or inadequate efforts to cope with contemporary stresses. Such patients should be referred for formal psychotherapy, if referral is possible, when their acute symptoms have subsided.

But "psychotherapy" in the sense of the physician's thoughtful effort to utilize information about the patient's personality, illness, and situation to maximize his therapeutic impact *during* the acute depressive crisis, must always be part of the treatment program of depressive episodes. Depressed people have an unsupportable burden of guilt, are convinced of their worthlessness and the hopelessness of their situation, and are unable to make decisions without great pain. The physician should avoid adding to these problems. Although he may himself be uncertain about outcome and procedure, the physician should avoid placing any responsibility for treatment decisions on the patient. Relating to the depressed patient in a sentimental, emotional or effusive way will in almost every case impair the physician-patient relationship. Exhortations, appeals to "willpower," moralizing, pontificating, and encouraging the patient to "snap out of it" will only add to his already overwhelming sense of guilt and worthlessness. Preferable but often difficult to achieve is a professionally competent, mildly formal, unsentimentalized attitude. One must beware especially of the tendency of older depressed patients to provoke in us feelings of pity and protectiveness, or their equivalent opposites, annoyance and rejection.

Occasionally, the family physician with long previous contact with the patient will know from the start or will soon learn that the acute depressive crisis is related to a specific psychological injury. This may be a personal, material or physical loss, or the loss of a *symbol* of personal, physical, or material strength. Retirement, bereavement, injury and illness are often associated with the development of acute depressions. In such instances, in addition to using the pharmacological and psychotherapeutic measures already outlined, the physician should encourage the patient to discuss his feelings about the loss. He should then consider, with the patient, what can be done to find substitutes and replacements for what has been lost. "Crisis-oriented psychotherapy"<sup>20</sup> is the more effective the sooner it is undertaken after the loss occurs; therefore it is often done more effectively by the non-specialist whose previous contact with the patient gives him earlier and more accurate clues about changes in the patient's life that are associated with the onset of depression.

Depressed patients make decisions poorly, and often with great pain. The patient's need to make decisions and his difficulty in responding effectively to that need can deepen his conviction about his own impotence and uselessness. For the acutely depressed the physician should simplify and reduce the need for making decisions by transferring decision-making temporarily to others, and by arranging to postpone decisions that cannot be transferred.

The informed collaboration of responsible relatives and friends can be invaluable assets in treatment if these people can be encouraged and taught to serve as companions to patients with a known but not prohibitive self-destructive potential. They can be "deputized" by the physician to stimulate the patient to maintain the normal routine of daily life. It is especially valuable for the physician to assure the patient and his family that bed rest is *not* necessary for the physically well but depressed, and can in fact be highly detrimental. The preservation of the patient's normal pattern—daytime: activity; nighttime: sleep—with conventional meals at regular mealtimes, minimizes the regression and social disruption which can develop in a depression.

Such measures can thus help to prevent both the physical deterioration and the destruction of habits and coping skills which will become increasingly important to the patient as he recovers.<sup>26</sup>

## Ambulatory Treatment of Acute Schizophrenic Episodes

Few would now contend that "schizophrenia" is a single disease entity, and most students of schizophrenia now agree that it has a complex, multicausal basis and a widely varied array of manifestations. However, the view that the several schizophrenic reactions have a common core of disturbances "in reality relationships and concept formations, with affective, behavioral, and intellectual disturbances in varying degrees and mixtures"<sup>10</sup> is widely held in this country. Most American psychiatrists would also agree that the schizophrenic reactions "are marked by strong tendency to retreat from reality, by emotional disharmony, unpredictable disturbances in stream of thought, regressive behavior, and . . . by a tendency to 'deterioration.'"<sup>10</sup> The standard subcategories of schizophrenic reactions (simple, hebephrenic, catatonic, paranoid and others) have little value in deciding upon treatment, and little relevance to outcome. They do not lead to useful choices among the kinds of treatment available.

A view of the schizophrenic reactions in which the subtypes are arranged along the continuum, "verbal and/or motoric activity," gives the physician with minimal academic interest in the problem of schizophrenia a useful guide to management and treatment:

### SCHEMA OF SCHIZOPHRENIC REACTIONS ACCORDING TO LEVEL OF ACTIVITY

withdrawn and depressed	perplexed and disorganized	delusional and hallucinative	excited and overactive
Low			High

Verbal and/or Motoric Activity Continuum

The nature of the symptoms and the social impact of an acute schizophrenic crisis will vary substantially, depending on whether the predominant symptoms of the episode are characteristic of the "low activity" or "high activity" extremes of the scale. In general, patients with symptoms characteristic of underactivity come to the attention of the physician later in the course of the episode because their disorder impinges less dramatically on the large and small social groups in which they live. Awareness of their symptoms as reflected in appropriate helping responses from the environment may, for such patients, be long delayed. Especially in those whose social contacts before the crisis were sparse and transient, the acute underactive schizophrenic episode may progress to-

ward a chronic state with no formal medical or public intervention. On the other hand, in the case of the acutely overactive, delusional, excited patient, even if his illness occurs in a social network characterized by impoverishment and impermanence of relationships, seldom does the condition go unrecognized; and almost always therapeutic effort of some kind is brought to bear. The term "acute psychotic crisis" almost always conjures up the image of an excited, delusional, perhaps threatening patient. To improve our detection of these episodes, it is important to keep in mind the frequency of psychotic crises that are characterized, instead, by withdrawal and inaction. Such patients have a strong proclivity for a quiet, socially "untroublesome" deteriorating course if untreated.

## The Overactive Schizophrenic Crisis

Beyond the matters of recognition and case-finding, the activity continuum has obvious implications for appropriate environmental-supportive responses, whose design and implementation can be one of the physician's most important contributions to the treatment of the patient with an acute schizophrenic crisis. The overactive, delusional and excited patient almost always has severely impaired judgment. Unless he is temporarily helped by others, his defective judgment may lead him to make decisions and engage in behavior consistent with his private perceptions but not with reality. Such behavior can disrupt his social relationships, impair his economic status and plant the seeds of later feelings of humiliation and self-doubt, all of which may outlast by far the acute psychotic episode itself. In many respects the schizophrenic patient who is overactive and overproductive resembles the acute manic patient and poses similar social and therapeutic problems. Similar efforts by the physician to encourage the collaboration of the healthier members of the patient's immediate social group are indicated. Such collaborators are not always available; they may already be too alienated or for other reasons disinclined to accept such roles. Or the patient's pathological activity and impairment of judgment may be such that the virtues of ambulatory care are overshadowed by its difficulties or dangers.

In such situations the physician can turn for help with treatment to public facilities and agencies. While these vary from community to community, they tend to include such services as psy-



chiatric clinic evaluations, voluntary day hospital or general hospital psychiatric units, and recourse through the courts for involuntary examination and treatment. Even in the case of the acutely excited or overactive schizophrenic, the patient's willingness to cooperate with the physician and accept his recommendations, and the availability of friends or relatives interested in the patient and willing to tolerate his pathological behavior for a while, can justify and recommend an effort at ambulatory therapy. In the absence of these conditions or in the face of the patient's unwillingness to use them, the physician should recommend to the patient, his family or friends that the patient voluntarily enter a hospital. Failing that, involuntary examination and treatment should be requested.

Should ambulatory therapy of the overactive schizophrenic patient seem feasible in terms of the criteria noted above, the physician will again find the phenothiazine drugs of special value. A parallel may be drawn between the activity continuum of schizophrenic symptoms and the stimulant-sedative continuum of the phenothiazine drugs, which may be charted as follows:

STIMULANT-SEDATIVE CONTINUUM OF PHENOTHIAZINE DERIVATIVES

<i>Stimulant</i>	<i>Mid-range</i>	<i>Sedative</i>
fluphenazine	triflupromazine	promazine (Sparine®)
trifluoperazine	perphenazine	chlorpromazine
	prochlorperazine	thioridazine

For example, the more potent, low-dose phenothiazine derivatives such as fluphenazine (Prolixin®, Permitil®) and trifluoperazine (Stelazine®) tend to have little sedative effect, and instead, may be mildly stimulating. They would, therefore, ordinarily be less effective for the rapid control of a hyperactive schizophrenic patient than phenothiazine compounds with some sedative action but without stimulating effects. Among the more sedative phenothiazines, chlorpromazine and thioridazine (Mellaril®) are outstanding examples. There is, in addition, a mid-ground of phenothiazine derivatives without either distinctly sedative or stimulating effects. Triflupromazine (Vesprin®), perphenazine and prochlorperazine (Compazine®) are examples of this middle group.

It is well for the physician to familiarize himself in detail with one representative of each of the three classes of phenothiazine compounds: the stimulating, the sedative, and the "middle" group. Taking chlorpromazine as an example of a seda-

tive phenothiazine, its appropriate dose range in the management of an acutely overactive, physically healthy young adult schizophrenic patient would be between 200 and 2,000 mg per day in divided doses. At the higher end of this range, concurrent administration of an antiparkinson compound is advisable because of the frequency with which uncomfortable but reversible extrapyramidal symptoms would otherwise develop.

There are problems associated with the high-dose administration of phenothiazine compounds. These include atropinic effects, hypotension, amenorrhea, weight gain, and, with prolonged use, pigmentary deposits in exposed skin, cornea and lens. These problems have received extensive but appropriate attention.<sup>5,16,22</sup> An entirely different problem associated with the use of phenothiazines in acutely psychotic patients has, however, received inadequate attention despite the fact that it has produced far more misery and far greater waste of human energy, time and material resources than all the forms of pharmacological toxicity with the phenothiazines. This is the widespread and strangely enduring tendency of inexperienced physicians to treat severely psychotic patients with inadequate doses of these drugs, and to withdraw or reduce the medication as soon as the patient shows a satisfactory response. Forrest<sup>13</sup> gave a dramatic picture of the consequences of this unfortunate tendency, which would certainly subside if more physicians understood that clinical improvement no more justifies cessation of phenothiazine therapy of a patient with acute schizophrenia than the achievement of a euthyroid state is an indication to discontinue thyroid supplement in the myxedematous patient.

In the younger acute schizophrenic patient with no history of previous psychotic crisis, maintenance phenothiazine therapy should be continued for six months to one year. In the older patient with a history of previous psychotic crises, especially if the earlier episodes have lasted for several months, it is advisable to continue phenothiazine maintenance dosage *indefinitely*.<sup>1,3,12,14</sup>

So much has been written regarding the techniques, indications and efficacy of psychotherapy with schizophrenic patients that even a summary of the subject would require volumes. For the purpose of this review, and with awareness of the extreme simplification involved, I would say that effective psychotherapeutic management of the acutely overactive schizophrenic patient depends



particularly on the physician's ability to preserve a clear image of himself as a physician treating an illness, and therefore willing to take an active and directive role in the patient's affairs as far as he must to protect the patient and hasten his recovery. At the same time he must recognize that this role is temporary and he must abandon it by stages in exact synchrony with the progressive return of the patient's ability to function without such direction.

Beyond that, after remission from an acute overactive schizophrenic crisis some patients express curiosity, and a willingness to learn about the interplay of the experiential, developmental and constitutional factors in the development of their illness with an eye toward reducing their vulnerability to subsequent crises. For these patients, referral for expert psychotherapy is in order whenever possible after the disorganization of the acute crisis is over. During the crisis itself, neither the patient's nor the physician's need to "understand" can be constructively satisfied.

#### The Underactive Schizophrenic Crisis

The withdrawn, underactive schizophrenic patient, when he comes to the attention of the physician, presents a treatment challenge quite different from that of the overactive patient. Apathy, anergy and indifference are the hazards, often along with profound depression and a crippling loss of responsiveness. Here, the physician's conviction that the withdrawal and alienation of the patient are symptoms, rather than choices, will usually lead him to take a position with the patient which communicates his expectation that improvement can be achieved and the patient restored to contact with his human environment. Fundamental to a helpful relationship with the withdrawn and apathetic schizophrenic patient is the physician's awareness that his patient fears and distrusts personal closeness. Thus, the physician must avoid being intimate, informal or too personal with the patient. Instead, the unsentimental, professional, somewhat formal approach described previously as particularly helpful to the severely depressed patient can be recommended, as well, for the physician undertaking the ambulatory treatment of a schizophrenic crisis characterized by apathy and withdrawal. Formal psychotherapy for such patients should not be attempted or evaluated until an adequate remission has been achieved, as with the overactive schizophrenic patient previously described.

Drug therapy for the withdrawn and underactive schizophrenic patient differs from that for the overactive, in that a rational choice of a phenothiazine agent would lead the physician to select a less sedative, more stimulating compound such as fluphenazine or trifluoperazine. Avoidance of parkinsonian side effects through the concomitant use of an antiparkinson agent is especially important with these phenothiazines. The inadequately informed physician tends to undertreat these patients, and to treat them too briefly. A typical dose of fluphenazine for such a patient would be 10 to 60 mg a day; of trifluoperazine, 20 to 100 mg a day. Again, adequate maintenance therapy should be continued, depending on the past psychiatric history, for six months to a lifetime after an adequate remission is achieved. The physician must bear in mind when treating withdrawn and apathetic schizophrenic patients with one of the low dose, high potency phenothiazines, that continued inactivity, disinterest and withdrawal are more likely evidence of inadequate than of excessive treatment.

Depression frequently coexists with the indifference, apathy and social impoverishment of these patients. Special consideration must be given by the physician to the risk of self-destructive behavior in any effort to treat them outside the hospital. Criteria similar to those previously outlined for the estimation of risk of suicide in psychotically depressed patients are applicable to inactive schizophrenic patients.

The role of supportive relatives and friends with the withdrawn schizophrenic differs from their role in the ambulatory treatment of overactive schizophrenics. With the apathetic patient, friends and relatives are of greatest value to the treatment program if they can be encouraged to serve as "extensions" of the physician by supervising the proper use of medication and helping the patient maintain reasonable patterns of hygiene, nutrition, sleep, physical activity, work and recreation.

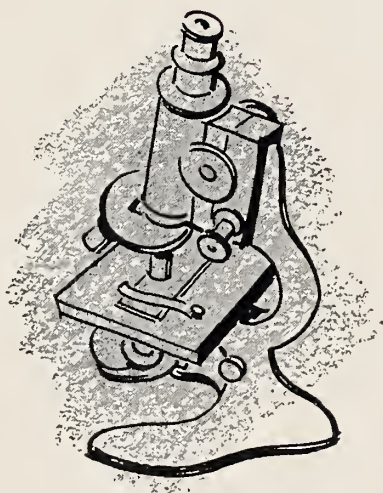
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# Hemorrhage During Long-Term Anticoagulant Drug Therapy

## Part II. Gastrointestinal Hemorrhage

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■ *Most of the gastrointestinal hemorrhages occurring during long-term anticoagulant drug therapy of 2,013 patients (reported in the literature) were caused by underlying lesions (44 of 77). Of the 44 lesions, only seven were diagnosed before treatment was started.*

*Most of the episodes of hemorrhage occurred with the prothrombin activity at a so-called "safe" level. Closer investigation before the anticoagulant therapy was begun might have brought the underlying lesion to light.*

GASTROINTESTINAL HEMORRHAGE is second to intracranial hemorrhage as the most serious bleeding complication during long-term anticoagulant therapy. Although it occurs more frequently and often is catastrophic in onset and severity, the mortality rate is low.<sup>1</sup> Controlled clinical trials have shown that anticoagulant drugs increase both severity and the incidence of gastrointestinal hemorrhage,<sup>2,3</sup> while similar studies of intracranial hemorrhage indicate that the use of anticoagulant drugs increases only the severity of the bleeding.<sup>2,3</sup>

This presentation is based on reports of 2,013 patients receiving long-term anticoagulant drug therapy (Table 1).<sup>4-11,13-18</sup> Some cases were reported as isolated instances and so were not analyzed in relation to the incidence of other hemorrhages.<sup>1</sup> There were 77 gastrointestinal hemorrhages (3.8 per cent) manifested by hematemesis or melena. The following questions are analyzed in this study:

1. What was the relation of gastrointestinal

hemorrhage to underlying lesions? How many lesions were recognized before treatment?

2. What is the relation of hypocoagulability in general to gastrointestinal hemorrhage?

3. What was the relation of gastrointestinal hemorrhage to "low" prothrombin determinations?

4. How many of the lesions could have been diagnosed before treatment?

*What Was the Relation of Gastrointestinal Hemorrhage to Underlying Lesions?*—In the 77 reported patients with bleeding episodes, causative lesions were diagnosed in 44 (Table 1). These were: peptic ulcer, 22; neoplasm, 8; diverticulitis, 4; hiatal hernia, 3; acute gastritis, 3; cirrhosis of the liver, 2; "inflammation," 2. The only lesions diagnosed before hemorrhage, however, were seven peptic ulcers. In eight of the 15 patients with peptic ulcers diagnosed only after hemorrhage, the diagnosis was based on roentgenographic studies and in seven cases it was made presumptively because of a typical history. In the 22 cases in which causative lesions other than peptic ulcer were diagnosed, the diagnosis apparently was made

This article on Hemorrhage During Long-Term Anticoagulant Drug therapy is in five parts. Part III is scheduled to appear in the March issue.

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TABLE 1.—Data from the Literature on Gastrointestinal Hemorrhage During Long-Term Anticoagulant Drug Therapy

<i>Authors</i>	<i>Cases Treated</i>	<i>Gastro-Intestinal Hemorrhage</i>	<i>Causes Given</i>	<i>Lesions Causing Hemorrhage</i>	<i>Identified Before or after Hemorrhage</i>
Tulloch and Wright <sup>15</sup> .....	227	6	2	Acute Gastritis Hiatal Hernia	After
Pollard, et al <sup>11</sup> .....	139	5	2	Duodenal Ulcer, both cases	Not stated
Nichol and Borg <sup>9</sup> .....	78	2	1	1 Duodenal Ulcer (1 Case x-ray after: negative)	Before .....
Suzman <sup>11</sup> .....	82	1	Not stated	Not stated	.....
Keyes, Drake and Smith <sup>7</sup>	121	3	Not stated	Not stated	.....
Pickering <sup>10</sup> .....	195	2	2	2 Peptic Ulcer	After
Bjerkelund <sup>2</sup> .....	119	7	7	4 Peptic Ulcer 1 Gastritis 1 Hiatal Hernia 1 Gastric Carcinoma	3 Before 4 After
Fisher <sup>5</sup> .....	195	8	7	7 Peptic Ulcers	After (by history)
Groch et al <sup>6</sup> .....	92	8	5	3 Neoplasm 2 Inflamm.	After
Borchgrevink <sup>3</sup> .....	103	3	3	1 Alcoholic Gastritis 1 Peptic Ulcer 1 Cirrhosis of Liver	1 Before "Hematemesis"
Waller <sup>17</sup> .....	275	11	2	2 Duodenal Ulcers	Before
Whittier et al <sup>18</sup> .....	54	8	3	1 Esophageal Varices 1 Duodenal Ulcer 1 Carcinoma of Colon	After
Stephens <sup>13</sup> .....	181	3	3	2 Diverticula 1 Gastric Carcinoma	After
Moseley <sup>8</sup> .....	62	6	5	2 Carcinoma of Colon 1 Diverticulitis 1 Duodenal Ulcer 1 Hiatal Hernia	After
Udall <sup>16</sup> .....	57	1	0	(Negative x-ray)	
Drinan et al <sup>14</sup> .....	33	3	2	1 Peptic Ulcer 1 Diverticulitis	After
TOTALS .....	2013	77	44		After 37 Before 7

from roentgenographic examinations. Among the 33 patients with no causative lesions detected, 15 had roentgenographic studies. Thus, causative lesions were found in nearly three out of four cases in which roentgenographic studies were made (37 of 52). The proportion of demonstrable lesions in studies of gastrointestinal hemorrhage occurring during short-term therapy is reported to be much lower.<sup>19</sup> Only seven out of 24 patients had demonstrable gastrointestinal lesions.

*What Is the Relation of Hypocoagulability in General to Gastrointestinal Hemorrhage?*—Controlled clinical trials leave little doubt that gastrointestinal hemorrhage occurs more frequently in a group of patients receiving anticoagulant drugs than in a control group.<sup>2,3</sup>

There is no precise test to determine the point at which failing coagulation will permit mild bleeding to become severe. A patient with normal coag-

ulation obviously can have a massive hemorrhage if an ulcer erodes a large blood vessel. The primary determinant of hemorrhage, thus, is not the coagulability of the blood but the nature of the vascular lesion.

For valid correlation of hemorrhage with clinical levels of prothrombin activity, it is necessary to know how much of the time during the total treatment period the prothrombin value was above and how much of the time below the "safe" level. The "safe" level was considered to be at or about 10 per cent by the prothrombin-proconvertin test or 20 per cent by the Quick one-stage test.<sup>1</sup> A low level observed after the onset of hemorrhage may be not the cause of the bleeding but the result of massive loss of blood which rapidly depletes the many thrombotic elements.

*What Was the Relation of Gastrointestinal Hemorrhages to "Low" Tests?*—Four studies were re-

TABLE 2.—Frequency of Spontaneous Gastrointestinal Hemorrhage in Long-Term Anticoagulant Drug Treatment in Relation to Times the Prothrombin Activity Was Below the "Safe" Level

				Prothrombin Tests*				
Authors	Diagnosis	Patients	Total	At "Safe" Levels	Below "Safe" Levels		Gastrointestinal Hemorrhage With number of Deaths in Parentheses	
					No.	Per Cent	At "Safe" Levels	Below "Safe" Levels
Bjerkelund <sup>2</sup> .....	Myocardial Infarction	119	11649	10654	995	8.5	2 (0)	5 (0)
Borchgrevink <sup>3</sup> .....	Angina Pectoris	103	2428	2115	313	12.9	1 (0)	1 (0)
Moseley <sup>8</sup> .....	Various	300	2668	2454	214	8.0	6 (1)	0
Askey <sup>1</sup> .....	Various	100	4326	3863	463	10.6	1 (0)	1 (1)
Totals.....		662	21071	19086	1985	9.4	10 (1)	7 (1)

\*Average interval between tests: Bjerkelund 1 to 3 weeks. Others, 4 weeks.

viewed in which all the prothrombin levels were stated during the total period of long-term treatment (Table 2). In 622 cases, 21,071 tests were made. In 1,985 test periods in which prothrombin was below the "safe" level, seven gastrointestinal hemorrhages occurred; in 19,086 "safe" periods, 10 bleeding episodes occurred. Lesions were demonstrated in all seven patients who had bleeding below "safe" levels and in nine of the 10 who bled at "safe" levels. Among those whose pro-

thrombin level was determined only after onset of hemorrhage, the correlation was comparable although not identical. There were 31 such patients in whom the cause of hemorrhage was demonstrated; in 20 of them the results of tests were at or above the so-called "safe" level (20 per cent Quick); in 10 of them below that level and in one equivocal (Table 3). It must be remembered that the "low" readings may have been the result of the bleeding and not the cause. Therefore the number

TABLE 3.—Relation of Prothrombin Activity to Gastrointestinal Hemorrhage With Underlying Lesions

Authors	Number of Cases	Lesions	Prothrombin Activity (After Hemorrhage)	
			In "Therapeutic Range"*	Below "Therapeutic Range"†
Tulloch and Wright <sup>15</sup> .....	2	1 Acute Gastritis 1 Hiatal Hernia	20 seconds (Quick) Equivocal ("25 to 40 sec.")	
Pollard et al <sup>11</sup> .....	2	Duodenal Ulcer	1, 19 seconds 1, 32 seconds (Control, 17 to 19 seconds)	
Nichol and Borg <sup>9</sup> .....	1	Duodenal Ulcer		35 Seconds (15% Quick)
Bjerkelund <sup>2</sup> .....	7	4 Peptic Ulcer  1 Hiatal Hernia 1 Gastric Cancer 1 Gastritis	1, Duodenal Ulcer, 11% PP  1, Hiatal Hernia, 10% PP	3 Peptic Ulcers (5%, 5% and 3% PP)  1 Gastric Cancer (3% PP) 1 Gastritis (7% PP)
Fisher <sup>5</sup> .....	4	Duodenal Ulcers	1, 28 Seconds (Quick)	1, 41.6 Seconds (Quick) 1, 150 Seconds (Quick) 1, 2% (Quick)
Groch, McDevitt and Wright <sup>6</sup> .....	5	3 Neoplasm 2 "Inflammation"	Inferred	
Borchgrevink <sup>3</sup> .....	3	2 Duodenal Ulcers 1 Esophageal Varix	1, 15% PP 1, 55% PP	1 Gastritis, 5% PP
Mosley, et al <sup>8</sup> .....	5	2 Colon Cancer 1 Diverticulitis 1 Duodenal Ulcer 1 Hiatal Hernia	"Not excessive"	
Drinan, et al <sup>4</sup> .....	2	1 Duodenal Ulcer 1 Diverticulitis	"In therapeutic range"	
Totals.....	31		20 (1 equivocal)	

\*At or above 10 per cent by prothrombin-proconvertin (PP) test or 20 per cent by Quick test.

†Below 10 per cent by prothrombin-proconvertin (PP) test or 2 per cent by Quick test.



of hemorrhages occurring at "safe" levels would be, if anything, higher.

Zweifler<sup>19</sup> reported comparable results in short-term anticoagulant therapy: Of seven patients with hemorrhage from demonstrated organic lesions, five had onset with prothrombin at or above 20 per cent (Quick test); of 16 gastrointestinal hemorrhages occurring at levels lower than 20 per cent, only two were due to lesions that could be detected roentgenographically. In other words, most of the patients with gastrointestinal hemorrhage in whom underlying gastrointestinal lesions could be demonstrated bled with the prothrombin activity at a so-called "safe" level. This was also true in recent reports.<sup>8,12</sup> The occurrence of only seven gastrointestinal hemorrhages during 1,985 periods when the Quick one-stage test was below 20 per cent hardly identifies this as an "unsafe" level.

*How Many of the Lesions Could Have Been Diagnosed Before Treatment?*—It is probable that most of the 44 lesions diagnosed after the hemorrhage could have been detected before the anticoagulant treatment was begun. Systematic search for such lesions before treatment was not reported in most of these studies. Many times the history recorded before treatment did not lead to suspicion of ulcers, although more intensive questioning following hemorrhage elicited a history of significant symptoms.<sup>5</sup> Many more of the 44 lesions that caused bleeding probably could have been identified (had they been suspected) from a more thorough inquiry and investigation before hemorrhage. Earlier recognition would ensure closer observation during treatment and would probably prevent many serious hemorrhages. Search for blood in the stool is a prerequisite to anticoagulant therapy, but in most of these patients it was not reported. The clinicians' uncertainty as to the accuracy and significance of stool tests for blood undoubtedly is responsible. If pre-treatment stool tests are repeatedly positive for blood, however, a thorough gastrointestinal investigation should be undertaken, even in the absence of symptoms.

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# Percutaneous Transhepatic Cholangiography

## Report of a Technique

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■ *Percutaneous transhepatic cholangiography was carried out in 30 patients with jaundice of unknown cause. The examination was successful in 24, and the correct diagnosis was established before operation in 23.*

*Among the specialized radiographic procedures useful in the differential diagnosis of jaundice, the percutaneous transhepatic cholangiogram is simple and reliable. It will distinguish intrahepatic from extrahepatic biliary obstruction. In benign structures, it can give a good anatomical and pathological definition of the problem which faces the surgeon. Occasionally, it may make operation unnecessary.*

*Serious complications are hemorrhage and bile peritonitis. The incidence is low and by careful management they can be avoided.*

TRANSHEPATIC CHOLECYSTOGRAPHY and cholangiography was introduced in Germany by Burkhardt and Muller in 1921.<sup>4</sup> It attracted little interest at the time and was completely forgotten with the discovery of intravenous cholecystography by Graham and Cole<sup>13</sup> by 1924.

In 1942 Carter and Saypol<sup>5</sup> having noted that bile was occasionally aspirated at liver biopsy, developed a technique for transhepatic cholangiography using a rigid No. 17 needle. A modification was introduced by Seldinger<sup>21</sup> in 1957 who covered an ordinary needle with tapered polyethylene tubing, and was thereby able to catheterize the biliary ducts.

### Selection of the Patient

When simpler methods of radiologic investigation are inconclusive, percutaneous transhepatic

cholangiography is employed to determine if jaundice is due to extrahepatic biliary obstruction.

The patient must be a suitable candidate for surgical treatment, and the examination is not done unless this requirement is met. Not all patients require surgical treatment, but they must be in condition to endure surgical operation should a complication ensue. The procedure is not done if the prothrombin time is less than 50 per cent. In the presence of a progressive fall in prothrombin time, the patient is first treated with vitamin K.

### Preparation of the Patient

Two ounces of castor oil are given the evening before to eliminate confusing shadows due to intestinal contents. For the same reason, the patient receives nothing by mouth for six hours before the examination.

Because of a high incidence of Gram-negative

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organisms during cholangiography,<sup>20</sup> the patient is given 250 mg of tetracycline every four hours for 24 hours before the examination, and this dosage is continued for 48 hours afterward. After the procedure has been explained to the patient, permission to operate is obtained. One hour before the examination, he is given 100 mg of pentobarbital (Nembutal®) and 5 mg of prochlorperazine (Compazine®) intramuscularly.



Figure 1.—Preliminary film of right upper abdomen with small lead marker placed on costo-chondral margin at mid-axillary line to indicate site of needle insertion. Duodenal loop opacified by 25 ml of Barotrast® to show the relative positions of the duodenum and liver edge.

## Technique of Catheterization

The odds in favor of successful catheterization are improved if the needle tip enters the area at the confluence of the larger intrahepatic biliary ducts. The liver hilum lies lateral to the duodenal loop, and its approximate position is determined by visualization of the duodenum.

To opacify the duodenum, the patient is given 25 ml of water-soluble iodide or barium and is turned on his right side for five minutes.

Then with the patient supine on the radiographic table, a lead marker is placed on the right costal margin at the mid-clavicular line. A preliminary film of the right upper abdomen is taken (Figure 1). From this, the relative positions of the opacified duodenum and the liver edge are known.

The angle for insertion of the needle is measured so that the tip will lie 2 to 3 cm to the right of the second portion of the duodenum. This angle varies with the individual and is usually somewhat toward the midline and about 45° from the horizontal (Figure 2).

After sterile preparation, the area for puncture is infiltrated with 2 per cent xylocaine. A small incision is made in the skin, and the subcutaneous tissues are spread by a hemostat to facilitate the passage of the needle and the catheter.

A 6-inch long, No. 15 gauge diameter Rochester needle with a tight outer covering of thin polyethylene tubing is utilized. While the patient holds his breath, the needle is passed rapidly to



Figure 2.—At left, the needle is directed so that the tip will lie 2 to 3 cm lateral to the duodenal loop. Right, depending on the habitus of the patient, the shaft of the needle forms an angle of about 45° with the horizontal.

the desired depth in the liver. The stylet is immediately withdrawn, leaving the outer polyethylene catheter in place. The patient may now breathe normally.

A clear polyethylene connecting tube filled with normal saline solution and a 10 ml syringe is attached to the catheter. As the catheter is withdrawn very slowly, an assistant exerts suction with the syringe. This is a painstaking procedure and is done with infinite care.

When bile is aspirated, the tip of the catheter is within a duct. If obstruction is of long-standing, white bile may be encountered. To make sure that the tip of the catheter is within the bile duct, about 5 ml of bile is aspirated and a similar quantity of 50 per cent diatrizoate sodium is injected. The biliary tree is then examined by fluoroscopy or polaroid filming.

If blood is obtained, a branch of the portal vein or the hepatic artery has been penetrated. The blood is flushed from the catheter, which is then withdrawn a little further so that the tip is no longer intravascular.

### Radiographic Technique

When it is certain that the contrast media enters the duct system, another 10 to 15 ml of bile is removed and an equivalent amount of contrast material is injected. A stopcock attached to the outer end of the catheter is closed. The patient is turned from side to side to promote mixing of the contrast media with the bile to obtain uniform filling of the biliary tree. Films are taken in the supine, 45° left anterior oblique and right anterior oblique, and in the prone position. At times, to eliminate obscuring shadows, a film is made in the upright position. Thirty-minute films are taken when there is a question of delayed emptying.

After satisfactory filming, the catheter is opened and allowed to drain. It is left in place to decompress the biliary tree. The open end is covered with a large gauze bandage, and nurses are instructed to change the dressing when it becomes soaked. The catheter remains in the bile duct until drainage ceases or the patient goes to the operating room. In one patient at Santa Clara County Hospital, the catheter continued to drain for three days. Shaldon<sup>22</sup> reported the catheter's being left in the liver for 14 days without complications.

The methods described by other investigators are similar.<sup>7,10,19</sup> Until Seldinger<sup>21</sup> employed a polyethylene catheter in 1957, all the procedures

were done with a solid 18 gauge spinal needle. Redington and coworkers<sup>18</sup> used a transthoracic approach. Fluoroscopy has been used as an adjunct to needle visualization by many investigators.<sup>12</sup> Some use injection while slowly advancing the needle into the liver substance. Now, roentgen television<sup>7,8,22</sup> has further advanced the technique.

### Radiographic Interpretation

In the presence of choledocholithiasis, the meniscus of the dye is concave downward, outlining the superior margin of the stone.<sup>14</sup> A small amount of the dye may pass around the stone into the duodenum (Figure 3). Slight to moderate dilatation of the common duct is seen. If the cystic duct and gallbladder are visualized, they frequently contain stones.

In bile duct carcinoma, there is a diffuse irregular narrowing of the involved duct with a dilatation of the peripheral portions.<sup>9</sup>



Figure 3.—Stone in the distal common duct. The patient, a 62-year-old woman, had had cholecystectomy and common duct exploration. A year later, upper abdominal pain developed. Transhepatic cholangiography shows a stone in the distal common duct with partial obstruction and reflux into the pancreatic duct. There is also filling of an adjacent duodenal diverticulum.





Figure 4.—Adenocarcinoma of pancreas obstructing common duct. The patient, a 66-year-old man, entered the hospital with a two-week history of jaundice. Serum bilirubin and alkaline phosphatase were elevated. Percutaneous transhepatic cholangiogram shows a complete obstruction to the distal common duct. At the point of obstruction, the duct is concave upward and the entire duct is decidedly dilated.



Figure 5.—Surgical stricture of hepatic duct. The patient, a 28-year-old woman, had had two operations. The first was for acute cholecystitis, and the second for common duct repair. A year later, she was admitted with jaundice. Percutaneous transhepatic cholangiography shows complete occlusion of the main hepatic duct at the confluence of the right and left branches.

With carcinoma of the pancreas or ampulla of Vater, the common duct is obstructed and the meniscus of dye is concave upward. The narrowed segment is funnel-shaped. Generally, obstruction is complete, with pronounced dilatation of the proximal common duct (Figure 4).

Intrahepatic tumor, whether primary or metastatic, results in extrinsic pressure on the ducts, causing the biliary tree to be distorted.

Stricture of the common duct is found at the site of previous surgical operation. There is a smooth narrowing at the site of stricture and pronounced dilatation of the proximal ducts (Figure 5). The examination is valuable in benign stricture, as it allows the surgeon to plan the most efficient type of anastomosis.<sup>11,19</sup>

## Results

Flemma and coworkers<sup>10</sup> reported 41 successful attempts in 46 tries. Three of the patients in whom satisfactory puncture was not obtained were later shown to have spontaneous clearing of jaundice. One was demonstrated at autopsy to have post-necrotic cirrhosis. Two were lost to follow-up. In Shaldon's series,<sup>22</sup> there were 22 successful punctures in 30 patients. Six in whom puncture was not satisfactory were shown at operation to have no extrahepatic obstruction. Kaplan<sup>15</sup> reported 40 cases, 32 of them obstructive in nature. He had 30 successful procedures. Atkinson's<sup>2</sup> review of the world literature up to 1960 showed an overall success of over 80 per cent. The relative success depends on the degree of duct dilatation, as was shown by Arner, Hagberg, and Seldinger.<sup>1</sup> Transhepatic cholangiography was successful in 50 of 56 patients with dilated ducts, but only in 19 of 46 patients with undilated ducts.

At the Santa Clara County Hospital, 30 patients were examined by percutaneous transhepatic cholangiography. The biliary tree was successfully opacified in 24 (Table 1). Of the six patients whose bile duct system was not visualized, four did not have extrahepatic biliary obstruction at operation. Most observers believe that if a duct is not entered after three or four tries, extrahepatic obstruction is unlikely.<sup>3,10,15,22</sup>

TABLE 1.—Results of Percutaneous Transhepatic Cholangiography, 30 Patients

Successful examinations .....	24
1 Correct diagnosis .....	23
Cholelithiasis .....	10
Carcinoma of bile ducts or gallbladder .....	4
Surgical stricture .....	2
Carcinoma of pancreas.....	5
Liver metastasis .....	2
2 Incorrect diagnoses .....	1
Unsuccessful examinations .....	6
(Diagnosis at operation)	
Cholelithiasis .....	2
Nutritional cirrhosis .....	1
Acute cholecystitis .....	1
Biliary cirrhosis .....	1
No diagnosis .....	1

## Complications

When the needle is passed into the liver, the patient has a sensation of mild discomfort. This is momentary and frequently there is no significant pain for the remainder of the procedure. Mild pain will occur if the contrast medium is injected into the peritoneal cavity or if there is a small amount of bile leakage. This is usually transient and clears rapidly.

Pushing the needle into the gallbladder is a complication which necessitates operation in most cases.<sup>16</sup> This accident, which occurred in three patients at the Santa Clara County Hospital, is immediately recognized by the aspiration of dark, viscid bile. When this occurs, the catheter is left in the gallbladder, and all the bile is aspirated. In one patient whose gallbladder was entered, the catheter was withdrawn immediately; bile peritonitis quickly developed, necessitating operation.

Elkington and Bernstein<sup>6</sup> found the incidence of bile peritonitis to be 6 per cent in 413 reported investigations. This they compare with the 3 per cent to 10 per cent surgical mortality of common duct exploration. The incidence of bile peritonitis can be reduced by allowing the catheter to remain in place until bile drainage stops or operation is done. Most complications occur in patients requiring more than one puncture.

Another serious complication is hemorrhage. Nearly always if operation is done immediately after the cholangiographic procedure, approximately 25 to 50 ml of blood is found in the abdomen. In one patient at the Santa Clara County Hospital, 500 ml of intraperitoneal blood was found, although no active bleeding was present. In this patient, the prothrombin time was low and the procedure was contraindicated. Careful evaluation of bleeding status should reduce this complication.

To date, two deaths attributable to this procedure have been reported. One was secondary to bleeding, and the other to bile peritonitis.<sup>17</sup>

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# Early Cutaneous Lupus Erythematosus

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■ *Cutaneous disorders which manifest themselves on the exposed parts are more likely than are hidden lesions to cause the patient to seek professional services promptly. Usually he consults his family physician or the community dermatologist. The physician who first sees the patient is dependent upon his own resources for management and diagnosis. A background of experience, a measure of energy and an inquisitive attitude are the necessary ingredients for successful management.*

*The difficulties involved in differentiating early lupus erythematosus and polymorphic light eruptions cannot be invariably resolved even with the most complete review. The course of the disorder and the response to environmental factors supply important clues. Investigative work, especially in the field of immunology, offers hope for the solution of some of our problems.*

THE FAMILY PHYSICIAN or the community dermatologist is often the first doctor consulted for a skin disorder which occurs on exposed areas. At a time when we strive to relate all or most of cutaneous disease to systemic disorders, we still find that the patient may be more concerned over the appearance of an eruption than he is with its cause or with many of his ills which are not so apparent. He may conceal or ignore a significant part of his history, but a bright red spot on his nose or cheek will often cause him to seek medical advice. Fully developed discoid lesions of lupus erythematosus offer no diagnostic difficulty, but even the experienced clinician will find that small infiltrated plaques, or an annular erythematosus lesion which may be transient, can afford a more difficult problem.

An example is a patient with diffuse erythema-

tous dermatitis involving the exposed parts, especially the face, perhaps of recent origin. The terrain of the scalp and the face may be seborrheic and the patient in the climacteric decade with early rosacea and concomitant seborrhea. This offers no difficulty if the story ends at this point. Unfortunately, such an eruption can be accompanied by symptoms which suggest systemic involvement. Recurring erythema, a history of febrile episodes at irregular intervals, a loss of weight, fatigue, pain in the joints and perhaps a history of rheumatic fever will suggest that the erythema is not banal.

It is more likely, however, that the patient will be a healthy young adult, perhaps a man, and an active one who plays golf and enjoys outdoor sports and is, therefore, much exposed to the sun and the weather. If the eruption were transient it would likely be ignored; but say it is persistent, occurs on his face and is therefore disfiguring. It is

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frequently asymptomatic and he may give a history indicating the onset of the disorder following intense exposure to the sun. In any event, in the absence of atrophic changes and follicular dilatation, we are likely to designate such lesions as polymorphic light eruptions. This group name was suggested by Haxthausen,<sup>6</sup> in 1929, to cover a group of recurring disorders in which exposure to sunlight is a significant part of the patient's story. Although the eruptions so classified can be persistent, they are often seasonal and they may involute spontaneously and recur, with or without subsequent undue exposure. The lesions have a characteristic distribution, occurring on the malar eminence, or the temporal areas, the nose and, at times, the postauricular regions. These areas of the skin are most exposed to the effects of sun, and, of course, this includes the sites in which lupus erythematosus most frequently makes its first appearance. If the process is initially non-destructive, the clinician may find that he has difficulty in establishing the diagnosis and he resorts to other procedures to support his clinical impression.

Histologic examination of the tissue involved is often the first recourse. Unfortunately, these lesions are frequently located in such a position that the clinician is loath to remove a big enough specimen for examination, and this is particularly true when the area involved is the nose. At an early stage, the histopathologic features may not be adequate to make it possible to differentiate between some of the manifestations of polymorphic light eruptions and the early erythematous nondestructive lesion of lupus erythematosus. The changes associated with chronic actinic exposure are frequently present in these sites of election. Liquefaction degeneration may be so slight that it does not offer a strong diagnostic clue, and the same may be true of the pattern and arrangement of the lymphocytic infiltration.<sup>7</sup> In Florida, we do not observe the plaque-like lesions with the same frequency with which they are reported from the Southwest and the Mountain States, nor even as frequently as they occur in the East and the Midwest. A diffuse erythema and an eczematous response is more likely to follow an undue or initial exposure to the sun in the Florida area. Vesiculobullous eruptions and recurrent summer prurigo, which are not manifestations of porphyria cutanea tarda, are rare indeed.

In Florida, we have the opportunity of seeing

patients who come during the winter season and it is not unusual to obtain a history which indicates that dermatitis will develop following the first exposure to sun on each of their winter trips. This may be a counterpart of the recurring summer eruption which occurs in a climate with seasonal changes and it may be the result of a sharp erythematous response following a period in which the skin has received little or no ultraviolet radiation. Often such a person first notices the eruption on the left arm as he drives down to Florida—an event which may not be so frequent now that many automobiles are air-conditioned. While some of our winter guests are plagued with persistent difficulty during their vacation period, others tend to improve following the initial exposure and reaction. More often than not the eczematous response is temporary and transient, the eruption soon disappearing not to return until the following year, even though the patient may be further exposed to a greater or less degree during the remainder of a vacation.

A vacationer with severe sunburn may simply purchase a proprietary remedy. Hotel physicians treat sunburn, but very few consult a specialist for a disorder in which the cause is evident. As the erythema subsides, a persistent papular eczematous response, which is not anticipated or which persists for an indefinite period, will often cause the patient to seek medical advice. This may be one of the transient forms of eczematous eruption which follows sun exposure, or it may be a papular or papulovesicular eruption which morphologically simulates miliaria rubra. As the patient perspires freely in the warm and humid climate, the erythematous response and edema may cause closing of the pores until the superficial layers of the epidermis are exfoliated.<sup>10</sup> This, at times, is a reasonable explanation for a part of the transient eruptions which follow sunburn.

Each observer develops opinions which are based upon his experience or that of his associates, and the data accumulated tend to color his observations, even though it may not rest upon an adequate statistical sample. In a 30-year experience with the diagnosis of eruptive disorders that may simulate lupus erythematosus, I find that I have designated one in seven of the circumscribed plaque-like erythematous eruptions as P.L.E. (polymorphic light eruption) and this disorder is usually the main stumbling-block in arriving at a definitive diagnosis. My group of 427 patients in-



cludes 347 with lupus erythematosus in which there were only six who were known or found to have systemic lupus erythematosus at the time of examination or subsequent observation. There were 80 patients in whom the diagnosis of polymorphic light eruption was considered to be a better designation. Infiltrated lesions which occur at the sites of election for these two disorders are more likely to be considered as a localized form of lupus erythematosus. The relationship of this disorder to light sensitivity is not so clear-cut as is that of the polymorphic light eruptions in which the prognosis and response to treatment is better. The association of lupus erythematosus with light sensitivity rests largely on the tendency for exacerbation which follows sunburn; and this, of course, may be interpreted as isomorphic response and a question can be raised concerning the etiological significance of such reactions. We have all observed patients with chronic discoid lupus erythematosus who endured exposure to light in their daily occupation without apparent detrimental effects. Furthermore, such eruptions frequently occur on the scalp and on the inner surface of the pinna of the ear, on covered parts and in the mouth, where sun exposure is hardly a significant factor.

Cutaneous manifestations of systemic lupus erythematosus are fortunately far less common than the eruptions which we have previously discussed. It has been known for many years that systemic manifestations which prove fatal develop in some patients with the chronic form of lupus erythematosus. Since the systemic form of this disease is frequently fatal, we can rely on past statistical reports and predict that only a small fraction of patients in whom classic discoid lesions develop will die of systemic manifestations of the disorder. It would seem almost as if the development of chronic discoid skin lesions reflected some measure of favorable immune response, or that they result from some factor which selects a less vulnerable organ in which to manifest itself.

A recent statistical analysis of a large group of patients with systemic lupus erythematosus indicates that only one in 10 has a chronic discoid lesion from the onset of the disorder, and that in less than a third will lesions of this type develop during the course of illness. These facts should stimulate us not only to a thorough study of patients with classic signs of the disease, but should spur us to extend our effort to appreciate and

record the ill-defined clinical manifestations in patients with the borderline signs of relative leukopenia and elevated sedimentation rates, in those with albuminuria and protein changes and those who have febrile episodes of undetermined origin, joint pain, low titer reactive serological tests, and other ill defined manifestations which may suggest systemic involvement. The recent carefully prepared statistical report on the cutaneous manifestations of systemic lupus erythematosus by Tuffanelli and Dubois<sup>11</sup> should alert each of us to study our ambulatory patients with greater care.

Those who have practiced dermatology for 20 years or longer can measure our advance of knowledge by reviewing the problems which concern the diagnosis and treatment of lupus erythematosus and the increase of interest in the light sensitive dermatoses. The initial work of Hargraves<sup>4</sup> and the subsequent modification of the L.E. test by Haserick<sup>5</sup> and others supplied us with a procedure which is a landmark in the development of this field of study. We soon found this test was routinely negative in patients with discoid lupus erythematosus, that it was frequently positive when there were systemic manifestations of the disease, and that the test was not entirely specific, for a positive reaction could be produced by a drug, hydralazine, used in the treatment of hypertension. Also, the test might be positive in a wide variety of disorders not previously suspected of bearing any relationship to the condition we now designate as systemic lupus erythematosus.

Practicing dermatologists primarily interested in ambulatory patients who present the early lesions of the disorder, received little help from the L.E. procedure, insofar as diagnosis was concerned. It did afford them a point of entry to expand their knowledge regarding the underlying mechanism involved in the production of this protean disease, and it offered a prognostic reference point. Continued immunologic investigation into the concept of auto-immune response may offer us the means of differentiating between the early lesions of L.E. and P.L.E. when the cutaneous manifestations may be morphologically identical. The L.E. cell factor which has been demonstrated to be a gamma globulin was one of the first known antinuclear antibodies. Such antibodies have been found in a wide variety of diseases—including systemic lupus erythematosus, in which they occur more frequently than in any other condition. Methods for demonstrating such antibodies by immuno-

fluorescence have given results which may be of considerable significance. With such methods, antinuclear antibodies have been reported as present in 90 per cent of the patients with S.L.E. and more than 50 per cent of patients with discoid lupus erythematosus, as well as being frequently positive in a number of related disorders and a wide variety of other conditions, but absent in patients with typical polymorphic light eruptions.<sup>8</sup> If a simple and reliable technique for the demonstration of antinuclear antibodies is developed, it can not only advance our understanding in the development of these disorders, but also help the clinician with early recognition of these conditions.

The clinical evidence that light is the precipitating factor in polymorphic light eruptions is good indeed, and experimental production of lesions identical with or simulating those present has been obtained by a number of investigators using artificial sources of light.<sup>1-3</sup> Each of them has found that it requires a sharp erythematous reaction to evoke the response—several minimal erythema doses—and, therefore, it can always be contended that this represents iso-morphic response. Other investigators demonstrated that reactions of similar, but not identical, character could be evoked in test subjects who did not have polymorphic light eruptions and whose skin was apparently normal.<sup>9</sup> An appropriate source for light testing must exclude wave lengths below 2,800, which do not occur in the earth's atmosphere, and furnish approximately equal amounts of energy between 280 and 320 m $\mu$  and longer wave length ultraviolet above 340m $\mu$ . A majority of available sources of ultraviolet energy do not supply the major components of natural sunlight. The carbon arc lamp using National Carbon projection carbons is reported to most closely approximate sunlight, if the wave length below m $\mu$  are removed by appropriate filters.

The shadow of incomplete knowledge falls across many of the problems facing the clinician. He struggles to arrive at a correct solution and a definitive diagnosis for a condition in which he can observe only the surface and speculate upon the underlying mechanism which produces these visible manifestations. He must explore the patient's past history to extract items of significance which lie buried because of lack of perception and the passage of time. Even the acquisition of knowledge regarding recent events and recent treatment can be difficult. How many patients do you have who

arrive at your office with a full sack of drugs previously used and an outline of their former treatment? If you have one, contrast him to the score you may see who are changing physicians hoping to find one who is clairvoyant. With problems presenting so many facets, it not infrequently appears that he is successful.

Each of us who devotes a major part of his time to clinical medicine will appreciate the changing spectrum in the diagnosis and treatment of many diseases. He must learn to evaluate his own observations on ambulatory patients and to contrast them with those of the clinician who works with institutional or clinic groups where a much larger number of late, fully developed and even terminal cases are under observation, investigation and treatment. It should be obvious that the findings in a terminal case will be more closely correlated to the findings at necropsy. It should be no less obvious to the final consultant and the pathologist that many of the changes present would not have been evident had the patient died from some other cause five, 10 or 15 years earlier. This is the problem that confronts us all with chronic illness and it is a major one creating diverse opinions among physicians who observe conditions early as they first appear; later, as they pass in full review; and, finally, when the disorder is terminal.

How does one accumulate statistical data on patients who recover, with or without treatment, or on those whose manifestations are minimal, or those where the disorder becomes stationary and the patient lives a normal span and dies of some other cause? It is this group of patients with the minimal and the early manifestations that presents the diagnostic problems. It is in this group that we need additional and better methods for diagnostic approach, inexpensive procedures that are not time-consuming, if such can be devised.

Methods of treatment will improve only with the accumulation of knowledge and its application to the alleviation of disease in the patients we treat. There is no condition in which empiricism has played a greater role in treatment than the disorder which is still designated as lupus erythematosus. Our knowledge of its protean changes, of the genetic determining factors and of the immunologic alterations is indeed rudimentary. It cannot be otherwise until methods are developed which will make it possible to extend the initial studies to an increasing number of patients who



are not disabled or in hospital. An adequate background of experience is not acquired until new tests and procedures for any disorder are widely used and evaluated, modified or discarded by an expanding number of investigators and clinicians. The lag between the investigative probe and its application to our daily problems is often a distressingly long interval.

Therapeutically, we again stand at the crossroads. The effectiveness of the antimalarial drugs in the control and suppression of the cutaneous manifestations of lupus erythematosus has been demonstrated. The untoward and detrimental effects of long continued treatment have come to light. Which of these drugs is the safer? When should they be used? Is there a total dose which should not be exceeded? Suppressive therapy with corticosteroids and agents which diminish the antigen-antibody reaction is now the treatment of choice for S.L.E. To what extent and in what manner can we use these agents in early non-disabling disorders? Does the correct topical and intralesional use of some of these agents pose any problems which cannot be anticipated? Only time, experience, and further study can answer these questions.

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# Renal Puncture

## A Neglected Aid in the Diagnosis of Renal Masses

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■ *Renal arteriography and nephrotomography are useful in distinguishing between renal neoplasms and cysts. In the great majority of cases the well-vascularized neoplasm is readily identified. However, the arteriographic diagnosis of an "avascular lesion" is incomplete. These lesions make up a widely heterogeneous group, including the common simple renal cysts, avascular and degenerated neoplasms and congenital malformations. Percutaneous puncture of these "avascular" lesions under image-amplified fluoroscopy is a safe and simple means of obtaining further diagnostic information, often of decisive value.*

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THE DIFFERENTIATION of carcinoma of the kidney from a cyst of the kidney is one of the more common problems facing the diagnostic radiologist. This is of more than academic interest, for many authorities now feel that the uncomplicated renal cyst requires no treatment. On the other hand, if carcinoma of the kidney can be diagnosed preoperatively, the kidney and the tumor can be removed intact without biopsy at the operating table.

The probability of a cyst and a neoplasm occurring in the same kidney was recently examined in a review of 1007 kidneys removed for a renal mass at the Mayo Clinic.<sup>7</sup> The incidence of co-existing cyst and neoplasm was 1 per cent. In no case was a carcinoma found inside a serous cyst that contained clear fluid.

Most of us when confronted with a renal mass on urography will turn to renal arteriography or nephrotomography to distinguish between a neoplasm or a cyst. With optimal technique an accuracy of 90 per cent can be achieved. Most renal tumors are highly vascular and the demonstration of a vascular stain or pathologic change in vessels is reliable evidence of a neoplasm. The opposite finding—"no vascular stain or change in vessels; mass most likely cystic"—is made with less assurance. Arteriography and nephrotomography are therefore particularly effective in selecting cases in which operation is needed.

An approach that deserves wider use is percutaneous puncture of renal masses. Sporadic series of renal punctures have been reported since 1939 with puncture limited to large, palpable masses.<sup>1,3</sup> In 1952 Lindblom described a series of 80 cases in which puncture was done under fluoroscopic control. This Swedish series has now

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been expanded to over 700 cases.<sup>6,5</sup> In this country DeWeerd<sup>4</sup> in 1963 reported the use of this method in 59 poor-risk patients without other evidence to suggest neoplasm. In a 1953 report on the inaccuracies of arteriography, Creevy and Price<sup>2</sup> made this statement: "The only dependable, nonsurgical means of recognizing simple cysts and those containing neoplasms consists of aspirating the cyst and replacing the fluid with contrast medium. . . . This method, however, is safe only with palpable masses, . . . [hence] a technique of limited applicability." Today, this limitation no longer holds, for with image-amplified fluoroscopy it is possible to direct a needle with great accuracy without excessive radiation exposure. In order to diagnose more completely the avascular renal mass, we have used this procedure in 25 patients since 1962.

**Technique.** After suitable premedication, 25 ml of methylglucamine diatrizoate is injected intravenously to opacify the renal drainage structures. The patient is then placed prone on the fluoroscopic table and the site of the mass is determined. The overlying skin and fascia are anesthetized and an 18- to 20-gauge needle of suitable length is advanced into the mass under fluoroscopic control. The mass is aspirated and any fluid obtained is sent for cytologic examination. The cavity is then filled with contrast medium and roentgenograms are made in various projections to outline its walls. The needle is then withdrawn and the patient kept overnight for observation.

## Reports of Cases

**Case 1.** A 50-year-old man had been discharged from the hospital three weeks previously following an uneventful recovery from operation for a herniated intervertebral disc. His present complaints were bilateral flank pain of three days' duration, with fever and chills during the last 24 hours. Temperature was 101°F, and bilateral costovertebral tenderness was elicited, somewhat more severe on the left. Urinalysis showed many bacteria and white cells. A culture of urine grew *E. coli*. A diagnosis of pyelonephritis was made and the patient responded promptly to antibiotic therapy. An excretory urogram was performed three days later, at which time the patient was afebrile and asymptomatic. This showed a 5 cm mass in the upper pole of the left kidney. Arteriography showed the mass to be avascular. Percutaneous puncture yielded 30 ml of thick pus. At operation an infected cyst was seen and *E. coli* grew on a culture of its contents (Figure 1).

**Case 2.** A 30-year-old woman was seen by her physician with complaints of gross hematuria, right flank pain and dysuria of 24 hours' duration. Microscopic examination of the urine disclosed many red and white cells. On treatment with sulfonamides the symptoms were promptly relieved. A subsequent excretory urogram demonstrated a 4 cm intrarenal mass on the left with calcification. Arteriography showed the mass to be avascular. On renal puncture the mass was found to be hard



Fig. 1.—(Case 1) Infected renal cyst. *Left and center:* Mass in superlateral aspect of left kidney detected on excretory urogram. *Right:* Delineation of mass following percutaneous puncture, aspiration of pus and installation of contrast material.



Fig. 2.—(Case 2) Renal hamartoma. Three urograms at top show irregularly calcified mass lesion at hilus of left kidney. The two frames at left below are arteriographs showing the mass is avascular. Lower right is a spot film showing tip of needle in solid mass lesion.

and noncystic. Operation disclosed an intrarenal mass of dense, partially calcified and hyalinized connective tissue, most likely representing a hamartoma (Figure 2).

Case 3. A 43-year-old woman was admitted to hospital with gross hematuria and right flank pain of four hours' duration. During the preceding six weeks, she had noticed a dull ache in the right flank, nausea and anorexia. She said she had not had fever. She had had episodes of urinary tract infection four and ten years previously which had responded to treatment with antibiotics. An excretory urogram performed elsewhere four years before was reported as showing no abnormality. Positive physical findings on admission were limited to temperature of 99°F and slight tenderness

in the right flank. Urinalysis showed many white cells. Leukocytes numbered 16,000 per cu mm. A mass at the upper pole of the right kidney was seen on an excretory urogram, and an arteriogram demonstrated that the mass was avascular. Renal puncture identified the mass as a dilated collecting system draining the upper pole of the kidney via a reduplicated ureter opening into the bladder neck (Figure 3).

### Complications

We have not observed any complications in our small series. However, since the technique is similar to that for needle excision for renal biopsy, the well-known complications of bleeding, infection and possibly arteriovenous fistula might be



Fig. 3.—(Case 3) Localized hydronephrosis. Film at left shows large mass involving superior pole of right kidney. Right frame shows percutaneous puncture of mass with instillation of contrast material to demonstrate obstructed collecting system to the superior pole of the kidney.



expected to occur. The incidence has proven acceptable in renal biopsy and an even lower complication rate would be expected in simple renal puncture.

The question of spread of a neoplasm by needle puncture cannot be answered simply. Needle excision of biopsy specimens from many kinds of neoplasms, such as those arising from the prostate, breast, head and neck, has been used for years. No difference in survival rates has been established between patients who had excision by needle and those who had other methods of biopsy or treatment.<sup>8</sup> Edholm and coworkers<sup>5</sup> noted a lower incidence of pulmonary metastasis in patients with kidney carcinoma who had renal puncture for biopsy than in those who did not. They conceded, however, that this might have been owing to earlier diagnosis. If puncture is limited to the mass already found avascular by arteriography, the only neoplasms punctured will be those that might otherwise have been misdiagnosed as "avascular, most likely cyst."

## Discussion

Our experience indicates that percutaneous renal puncture under image-amplified fluoroscopy offers a safe, simple method of increasing the accuracy of diagnosis of kidney masses. We use the following as guides in determining the use of the procedure:

- A renal mass that is obviously neoplastic on urography requires surgical treatment. Little additional useful information is to be gained by extensive radiologic investigation.
- The more common renal mass without identifying characteristics on urography should be first

studied by arteriography or nephrotomography. If a tumor stain or pathological change in vessels is demonstrated, the treatment is surgical. If neither of these conditions is demonstrated and the lesion is "avascular," percutaneous renal puncture will confirm the benign, cystic nature of the lesion or afford clues to a more specific diagnosis.

- Under special circumstances, such as in aged, poor-risk patients, where arteriography or exploratory operation may be contraindicated, renal puncture will usually give decisive information with minimal morbidity.

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# Pregnancy and Urinary Calculi

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■ *The possibility of upper urinary tract calculus disease is at least as great in pregnant as in nonpregnant women, and such disease if present carries greater risks during pregnancy. The well-being and even the life of both mother and fetus may depend on prompt diagnosis, the right kind of management and effective treatment. With adequate precaution, such essential procedures as urography and emergency surgical intervention can be carried out during pregnancy at little greater hazard than ordinarily attends them.*

IN THE PREGNANT WOMAN, two main factors enhance the dangers attendant on calculus disease of the upper urinary tract: (1) the physiologic changes associated with pregnancy foster the development of upper urinary tract dilatation, while the dilatation tends to obscure awareness of both patient and physician that a urinary calculus may be present; (2) treatment for urinary calculi during pregnancy poses special problems.

## Physiology

In 90 per cent of pregnant women, the superior two-thirds of the upper urinary tract undergoes dilatation; this impairs drainage and leads to urinary stasis, causing back-pressure in the renal pelves. The changes in the ureter are characterized microscopically by hyperplasia and hypertrophy of smooth muscle and connective tissue, plasma cell and leukocytic infiltration, increased vascularity, and edema. The irritability response of ure-

teral smooth muscle is reduced. The alterations become gradually more pronounced up to the seventh month, diminish during the eighth and ninth month, and are ordinarily followed by reversion to normal by the third postpartum month.

The alterations appear to be caused chiefly by hormonal and, to a lesser degree, by mechanical factors incidental to the pregnancy. The evidence for hormonal causation is circumstantial but strong. Certain of the urinary tract changes occur during the first trimester of pregnancy, before uterine enlargement is sufficient to produce mechanical obstruction. Van Wagenen and Jenkins<sup>8</sup> showed that the changes in the upper urinary tract persisted after the death or the surgical removal of the fetus, provided the placenta was left in place and active. Because the uterus and upper urinary collecting system have a common embryologic origin, the basic hormonal influence that produces reduced irritability, relaxation, atony and dilatation of the musculature in the gravid uterus also produces these same effects in the ureters and renal pelves. Evidence for the contribution of mechanical factors is the predominance of urinary tract changes on the right side, owing to dextroversion of the uterus,

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and the cushioning effect of the sigmoid colon on the left.

## Incidence

The likelihood that urinary calculi occur more frequently in pregnant than in nonpregnant women has been mentioned by Arnell and Getzoff,<sup>3</sup> who found an incidence in pregnant women of 1:852, which they believed to be twice the rate in nonpregnant women of the same age range. Scardino, Prince and Su<sup>7</sup> brought attention to the fact that urinary calculi are more common in the female at all ages than in the male, and suggested that this greater frequency is related to the higher incidence of urinary tract infection in females. These, and the following additional factors may explain why urinary calculi are more common in women than in men, and perhaps more common in pregnant than in nonpregnant women: Urinary infection has been reported to occur six times as often in pregnant women as in other adults;<sup>6</sup> this may represent a continuation of urinary tract infection that was present in childhood. Vesicoureteral reflux, found in about half of children with recurrent pyelonephritis, may be present during pregnancy and perpetuate urinary tract infection. Hutch and co-workers<sup>5</sup> found vesicoureteral reflux in a considerable percentage of women in whom pyelonephritis persisted postpartum. They expressed belief that the reflux had probably existed during pregnancy.

## Diagnosis

A calculus in the renal pelvis or ureter may cause little or no pain during and after pregnancy, since the structures are dilated and the sensitivity of the pelvic or ureteral wall is reduced by edema. If pain or aching is felt, it may be misinterpreted by both the patient and the obstetrician as being due to the pregnancy or to the associated laxity of ligaments or faulty weight distribution that are so common in pregnancy. Following delivery, the patient often neglects to seek treatment even though she may have been informed that a calculus is present. A patient in whom we discovered calculi during pregnancy waited seven years before requesting treatment.

The physician usually does not look for calculi in the urinary tract of the pregnant woman because he is reluctant to expose the fetus to radiation and because of the widespread recommendation that if

a stone is found in a pregnant woman it should be treated nonsurgically. In weighing these considerations the following factors should be taken into account:

1. The amount of radiation to which the fetus is exposed can be considerably reduced by the limited area urographic film technique,<sup>2</sup> and by shielding as much of the maternal pelvis as is feasible during urographic studies.

2. Since the period of highest incidence of production of gross anomalies in the human embryo as a result of exposure to ionizing radiation is believed to be the first month of intrauterine life, roentgenologic procedures should if possible be postponed until after this period.

3. For roentgen diagnosis in pregnant women suspected of having a stone in the upper urinary tract, we have successfully used a single anteroposterior film of the abdomen, taken seven to 10 minutes after the intravenous injection of contrast medium.

4. We have found double dose contrast medium excretory urography very helpful in the diagnosis of urinary calculi.<sup>1</sup> The prompt visualization that is afforded by this technique has enabled us to decrease the number of films made and to avoid making the delayed film. In our practice, combining this technique with limited area urographic filming has significantly reduced the radiation exposure of mothers and fetuses.

The possibility of renal or ureteral calculus must be considered in any pregnant woman with severe pyelonephritis or with abdominal pain. Pus cells are usually present in the urine, but the bladder urine may be clear if there is complete blockage on the involved side. The roentgenographic diagnosis may be difficult, since cystine and uric acid calculi are radiolucent, and fetal bones may confuse visualization of calculi. Radiopaque densities in the right upper quadrant of the abdomen may be in the kidney or in the gallbladder; differentiation may necessitate cholangiography in addition to excretory urography. The ureteral dilatation that is incident to pregnancy may permit calculi of much larger than average size to reach the lower portion of the ureter.

Occasionally the knowledge that a calculus is present may lead to the misdiagnosis of some other entity that is causing symptoms resembling those of urinary calculus disease. Thus, Barter and Rovner<sup>4</sup> observed a 48-year-old woman in whom the

presence of a ureteral calculus was known before she became pregnant and who was admitted to the hospital in the 36th week of gestation because of abdominal pain. The proper diagnosis—twisted fallopian tube—was obscured by the more obvious presumption of ureteral colic. Investigation for urinary calculi sometimes leads to the incidental discovery of gynecologic disease. While studying a patient with symptoms arising from a ureteral calculus, we noted a dermoid cyst of the ovary which had caused no overt difficulties, and which was later removed surgically.

## Treatment

A pregnant woman with a previous history of urinary calculi should take adequate fluids and limit the intake of calcium and vitamin D to the amount necessary for her needs and those of the fetus—not enough to cause hypercalcemia or hypercalciuria. It should not be overlooked that pre-existing cystinuria continues during pregnancy and that it is important to apply the usual principles of alkalization of the urine and urinary output exceeding 3,000 ml daily, in an effort to prevent calculus formation.

For the following reasons, nonsurgical treatment for calculi in the upper urinary tract may be detrimental to the gravid woman or the fetus: Premature births are more frequent in women with pyelonephritis than in those not so affected. Stones in the urinary tract aggravate and perpetuate pyelonephritis while impeding treatment and eradication. Advancing obstruction by one or more stones may irreparably damage renal function and increase the possibility of bacteremia and septicemia. In the young primigravida, congenital anomalies may be the cause of associated urinary calculi.

Surgical treatment, including removal of stones and relief of obstruction, may be life-saving. If, after consideration of all factors involved, surgical intervention appears warranted, there is no need to prolong suffering and disability by withholding the procedure merely because the patient is pregnant. Safety has been much increased by such devices as modern techniques of anesthesia, the judicious use of antibiotics and proper attention to fluid and electrolyte balance.

Each step in the surgical approach must be planned with special care. If at all possible, emergency procedures should be avoided. The patient's situation should be assessed individually. Proper

cooperation between the urologist, obstetrician and anesthesiologist is essential.

Several important factors influence the choice of procedure and the selection of the time to do it. The 18th week of gestation is optimal. By then, the shift in the site of estrogen and progesterone formation, from ovaries to placenta, is complete; the placenta is entirely formed and securely anchored. Before the 18th week, spontaneous postoperative miscarriage may take place because these processes are not yet complete. After the seventh month of gestation, the delivery of a viable fetus can be expected even if premature.

Preoperative preparation should include the administration of the usual sedatives the night preceding and on the morning before the surgical procedure. In most cases spinal anesthesia is preferable. Early postoperative ambulation should be encouraged.

Cystoscopic manipulation of calculi in the lower portion of the ureter may be difficult in late pregnancy, when the fetal head is pressing in the area of the bladder and the lower ureter. In advanced pregnancy, an impacted stone in the lower ureter may necessitate preliminary nephrostomy. When obstruction is bilateral, nephrostomy drainage through a polyethylene tube—a technique that continues to arouse controversy—may on occasion save life by enabling the urologist to postpone an operation that would have endangered both the fetus and the very sick mother. The technique was used successfully in two patients by a colleague.

Not to be recommended is vaginal removal of a lower ureteral stone, for a leaking urinary fistula may persist and vaginal delivery may be rendered more difficult. Some surgeons, in an attempt to delay definitive treatment during pregnancy, advocate pushing a ureteral calculus back into the renal pelvis. We avoid this if possible since there is no assurance that the stone will remain in the kidney. Once, in the case of a woman with twin pregnancy near term, we were obliged to push a stone in the proximal ureter into the renal pelvis, but we recommended that it be removed surgically during the puerperium. This advice was not followed.

Stones that produce obstruction at the ureteropelvic junction or that become impacted in the ureter present an emergency. If possible, the obstruction must be relieved first, by inserting a ureteral catheter into the renal pelvis. The catheter should be left in-dwelling. Once the symptoms are

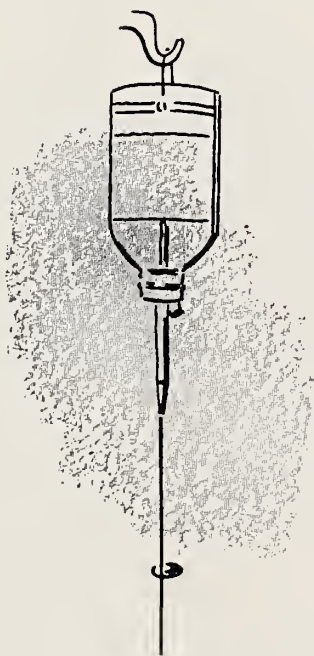


controlled and renal function restored, definitive treatment can be planned according to the size and position of the stone and the stage of pregnancy. If the ureteral stone appears to be small enough to pass spontaneously, it should be given an opportunity to do so, after an appropriate interval during which drainage of the kidney and dilatation of the ureter are facilitated by the use of an in-dwelling catheter. Stones that are too large to pass spontaneously must be removed surgically. The procedure may be performed during pregnancy; or, if gestation is near term, ureteral catheter drainage should be continued until after delivery. The stone may then be removed by operation or cystoscopic manipulation. A stone that is causing complete obstruction, and that cannot be bypassed, demands immediate surgical removal regardless of its size or position.

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# Decompression of the Facial Nerve

## A Surgical Emergency

LEE SHAHINIAN, M.D., *Los Altos*

■ *The chance of return of normal function in cases of facial paralysis is enhanced by early surgical decompression and repair of the facial nerve.*

*Modern precision testing is of considerable aid in prognosis as well as diagnosis. Faradic testing and electromyography can offer relatively early information as to the possibility of permanent facial deformity. Now that microscopic surgical techniques have considerably facilitated operations on the facial nerve, early operation is the treatment of choice in such cases.*

FACIAL EXPRESSIONS often play an important role in revealing character and personality. With facial paralysis, the detracting effect is relatively minor during facial repose, but when the affected person smiles, what would ordinarily be an expression of friendliness or merriment may become a twisted leer which seems to express cynicism.

The following table by Cawthorne shows some of the causes of facial palsy encountered over a period of 20 years.

<i>Causes of Isolated Facial Palsy</i>		
	<i>No. of Cases</i>	<i>Per Cent</i>
Idiopathic .....	473	64
Injury .....	119	16
Geniculate .....	61	8
Infection .....	42	5
Neoplasm .....	28	3
Nuclear .....	12	1.5

The indications for surgical correction in cases of paralysis caused by injury, infection or neoplasm have been much more definite in the past than for paralysis caused by so-called idiopathic factors. This article is primarily directed toward this latter group and to support of an opinion, that earlier surgical intervention is advisable in selected cases.

Presented before the Section on Ear, Nose and Throat at the 94th Annual Session of the California Medical Association, San Francisco, 28 to 31 March 1965.

Briefly, the diagnosis of idiopathic or Bell's palsy should be restricted to cases in which the facial palsy is the only clinical symptom with no obvious cause to be found on examination.

The facial nerve lies in a narrow, tortuous tube encased in the temporal bone. Any reactive swelling of the nerve or its sheath may squeeze the blood out of the vessels which nourish the nerve and thus deprive it of the oxygen vital to its function. The chain of events in Bell's palsy is as follows: Primary ischemia caused by vasospasm results in venous stasis and edema of the facial nerve within the facial canal. The edematous nerve in turn causes secondary ischemia, with further impairment of circulation. Oxygen deprivation is the result of the vicious cycle thus established.

Inasmuch as many patients with Bell's palsy recover completely without medical or surgical intervention, neurologists in most centers have for many years advocated watchful expectancy. However, the patient who does not obtain satisfactory return of function, after months of agonizing suspense, receives little comfort in knowing that in most similar cases the patient fared better.

Refinement of diagnostic methods and concepts in recent years have made possible more precise prognostications and therapeutic indications. Electrodiagnosis has become increasingly useful in determining the extent and severity of the under-



lying physiological disturbance. Absence of faradic reaction (interrupted current) suggests early Wallerian degeneration. If there is no galvanic reaction (continuous current) muscle atrophy is indicated. When no contraction is present with either current it is because the reaction of degeneration has occurred. Electromyography provides further confirmation of reaction of degeneration if fibrillations occur on the tracings.

Cawthorne<sup>2</sup> reported that patients with incomplete palsy, as determined by clinical and electrical findings, have a relatively good prognosis without special therapy. Ninety-five per cent of these patients recover spontaneously. However, those who have complete palsy, with proven reaction of degeneration, have a much less favorable prognosis without surgical therapy. Only 45 per cent of such patients recover completely. Thus, with nerve conduction tests it is possible to predict which patients may recover quickly and completely and which slowly and not fully.

Electrodiagnostic studies are indicated at twice weekly intervals following the onset of the facial paralysis. Should reaction of degeneration occur, immediate surgical decompression of the seventh nerve is indicated. Kettle<sup>3</sup> and others have demonstrated that the prognosis for return of function is greatly enhanced with such a course of action.

The advent of microscopic surgical techniques has greatly increased the confidence and competence of otologists working in the region of the facial nerve. Exposure and decompression of the nerve is no longer a formidable task. Some difference in opinion exists as to which surgical approach, endaural or post-auricular, is most satisfactory. The endaural approach offers the best view of the nerve where it first makes its descent in the vertical portion of the canal. On the other hand the post-auricular approach is advantageous because the stylomastoid foramen can be enlarged much more easily and this is the most important part of the procedure of decompression. Inasmuch as incisions in and about the ear heal so nicely, I make use of a combination of both incisions in order to obtain optimum working conditions in all areas. Ten power microscopy is used for examining the operative field during the initial exposure of the nerve with a 4 mm motor-driven burr. In the process of bone removal there is a stage just before actual exposure of the nerve when a reddish streak appears that indicates the proximity of the nerve sheath. That is the point at

which the bony covering of the canal has been reduced to a fraction of a millimeter in thickness and is sufficiently translucent to make the underlying vascular structure of the nerve sheath visible. A smaller burr is then used to lathe a sulcus parallel to the nerve on either side of its entire vertical portion, almost exposing the sheath. This hollow grinding technique makes it much easier to make gentle use of a small stapes curette to remove the final layer of thin bony plate overlying the sheath. Three-quarters of the nerve circumference is thus exposed. The compressed blood vessels thereupon fill with blood and the nerve bulges to varying degrees. Care must be taken to carry the decompression well into the stylomastoid foramen. I do not slit the sheath and I cannot see the rationale of doing so if the nerve is otherwise adequately decompressed. The incisions are closed without drainage after the nerve is covered with Gelfoam pledgets and a fascia pedicle is dropped into the inferior portion of the mastoid cavity.

### Reports of Cases

CASE 1. A 16-year-old boy, examined on referral 15 November 1963, had awakened nine weeks previously with pain at the base of the skull. He noted that he could not move the left side of his face. The pain disappeared shortly but the sense of taste was impaired for about a week. A neurosurgeon attending the patient ordered electrodiagnostic testing at intervals by a qualified physiatrist. These examinations indicated gradual deterioration of the facial nerve to a stage of complete reaction of degeneration.

Surgical decompression of the facial nerve was performed on 19 November, approximately 10 weeks after onset of the paralysis and one week after complete reaction of degeneration was first noted. The nerve sheath was well exposed from the level of the horizontal semicircular canal to the digastric groove. The sheath was bright red in color but bulged only slightly when freed from its bony prison. No attempt was made to achieve further decompression by slitting the epineurium. Gelfoam pledgets were used to cover the nerve and a fascia pedicle was draped into the mastoid cavity. The skin incisions were completely closed and the patient was sent home two days after operation. Electrical stimulation was begun again 10 days after operation and encouraging responses were noted a few days later and within a month voluntary movements of the affected side were

easily detectable. The attending neurosurgeon prescribed the use of a small Waters electrical stimulator for home use, and when the patient was seen two months later most of the facial function had returned except that the patient could not wrinkle the left side of his forehead and had to concentrate to completely close his left eyelid. The latter function thereafter gradually improved but the forehead musculature remained immobile.

CASE 2. A 42-year-old woman who was examined on referral 15 January 1965 had wakened approximately seven weeks previously to find that she had difficulty in moving the left side of her face and could not close her left eye. She immediately saw an internist who prescribed vitamin B-12 and referred her to a physiotherapist for treatments. As the treatments did not help, the patient was referred to me for opinion and therapy as indicated. Electrodiagnostic tests performed on 18 January disclosed complete reaction of degeneration and fibrillation to electromyography. Decompression of the facial nerve was carried out the following day, almost two months after the onset of symptoms. Excellent exposure of the nerve was accomplished without difficulty. The sheath was quite red, moderately swollen and trabeculated, with small vessels on the surface. No attempt was made to decompress the nerve further by slitting the sheath. Gelfoam strips were used to cover the nerve and the incisions were completely closed. The patient was sent home after two uneventful postoperative days. Eight days after operation, barely perceptible voluntary twitches could be noted in the corner of her mouth. Facial function then steadily improved to the extent that, less than two months after operation, all natural facial

creases were present. Home use of a small Waters electrical stimulator was prescribed for supplementary exercise several times daily.

## Discussion

Ordinarily, in cases in which complete reaction of degeneration occurs, beginning signs of recovery are not expected for seven to nine months. In the cases here reported, recovery began much sooner—three weeks after operation in one instance and only one week afterward in the other.

Certainly in any case of idiopathic facial palsy medical care should be instituted as soon after onset as possible, with use of nicotinic acid and corticosteroids to bring about vasodilation and reduce secondary edema. Some investigators advocate supplementing such a program with the use of stellate ganglion block, a procedure with which I have had no experience. Clinical observations should be correlated with serial nerve conduction tests and electromyography. Should deterioration of function continue to the extent of complete paralysis and reaction of degeneration, surgical decompression should be performed without delay.

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# CASE REPORTS

## Disseminated Cryptococcosis

### Multiple System Involvement; Preoperative and Postoperative Therapy with Amphotericin B and Removal of a Pulmonary Lesion

R. L. STIRRETT, M.D., *Arcadia*

CRYPTOCOCCOSIS IN HUMANS may persist for a time in a localized form and then heal spontaneously or continue locally with possible progression and ultimate systemic dissemination.<sup>3</sup> The disseminated form may affect almost any organ system and until recently it has been regarded as nearly always fatal, particularly if the central nervous system is involved. Remission and exacerbations are characteristic of the disease in any form. In an excellent review of the disease, Littman<sup>7</sup> called attention to the increasing incidence of the disease among psychiatric patients.

In light of the growing number of reports from large centers<sup>4,7,10,12,13</sup> of amphotericin B therapy of disseminated cryptococcosis, it might seem that reports of isolated cases would be of decreasing interest. However, as the number of cases from any one institution is still likely to be relatively small, the pooling of data on all cases of central nervous system cryptococcosis still seems advisable. The reports available on such cases show wide divergence of opinions on methods and effectiveness of treatment. Factors involved include:

- **Dosage.** Furcolow<sup>4</sup> expressed the belief that the administration of a total dose of less than 2 gm of amphotericin is not advisable because of the likelihood of relapse,<sup>4</sup> but other investigators hold that relapse is not related to the amount that was given to obtain remission.<sup>13</sup>

- **Intravenous administration.** The administration of amphotericin on alternate days is advocated<sup>1,13</sup> as a way to make the unpleasant reactions less severe and of course less frequent without sacrifice of adequate blood and spinal fluid levels of the drug. It has been noted also that the toxic effects of amphotericin—renal damage as manifested by uremia, hypokalemia and urinary abnormalities—and the side effects such as chills and fever are less frequent when the drug is infused on alternate days.<sup>1,7</sup>

- **Intraspinal and other modes of administration (intracisternal, etc.).** These methods have been found to result in higher spinal fluid levels of amphotericin than are produced by intravenous infusion, and they have been advocated<sup>13</sup> for patients who cannot tolerate or do not respond to intravenous treatment.

- **Surgical excision.** In one report<sup>10</sup> cryptococcosis was found to be the etiologic agent in five previously undiagnosed local pulmonary lesions that were surgically excised. In one of these cases, cure without subsequent amphotericin therapy was reported. Other investigators<sup>3,7,8</sup> have expressed favorable opinions of excision of local cryptococcal pulmonary lesions. The value of resecting pulmonary lesions when there is also central nervous system involvement is less well determined.<sup>5</sup> Katz and coworkers reported apparent remission in a case in which amphotericin was given before and after excision of the lesion, and Kress and Cantrell<sup>6</sup> reported remission in a case in which the drug was not used until after operation.

The frequent association of cryptococcosis with Boeck's sarcoid (and to a lesser degree Hodgkin's disease) is often mentioned; it may be related to low resistance. Shields<sup>11</sup> reported a case in which cryptococcosis appeared to be the etiological basis for an extensive reaction of sarcoid type. The apparently close relationship between sarcoidosis and cryptococcosis was referred to in a similar report by Bernard and Owens.<sup>2</sup>

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Submitted 2 December 1964, revised December 1965.

The case herein reported is the only one of record in any of three private hospitals, totaling about 700 beds, in the western portion of San Gabriel Valley. This might suggest either that cryptococcosis is not endemic in the area or that it is not being recognized. The great number of birds present throughout the year might suggest the latter. It has been suggested that complement fixation and skin tests, were they available, would facilitate the diagnosis and help determine the prevalence of the disease.

### Report of a Case

The patient, a 31-year-old Japanese woman, was examined by the author 18 August 1962 because of headaches of three weeks' duration. The headaches were described as intermittent, frontal in distribution, sometimes lasting as long as six hours. The patient felt that the headaches were brought on when her baby cried a great deal or when she was confronted with many activities more or less all at once. Taking salicylates did not often completely relieve the aching, and two days before she was seen by the author the patient had taken propoxyphene hydrochloride (Darvon®) on prescription by another physician. Nausea and vomiting followed, which the patient attributed to the drug. There was evidently no previous history of headaches, no impairment of hearing or of sense of smell or taste, no muscle weakness or sensory loss. There was, however, an indefinite history of double vision over many years, rarely occurring and always associated with excessive fatigue.

Two weeks before the onset of the present illness, the patient had a "sore throat" and consulted an otolaryngologist, who prescribed several courses of a "broad spectrum antibiotic" over a period of six days in addition to the use of salicylates. An eruption affecting the skin of the face appeared during this time and the patient consulted a dermatologist who intimated that the condition might be caused by the salicylates. As an alternative he then prescribed propoxyphene hydrochloride, as already mentioned.

The patient had three siblings who are alive and well, in Japan. Her father had died there two years before the onset of the present illness, of lung cancer confirmed at autopsy. The patient's mother was said to have "cancer of the pelvis." There was no other family history of cancer, diabetes, tuberculosis, epilepsy or mental illness.

The patient said that she had been born and

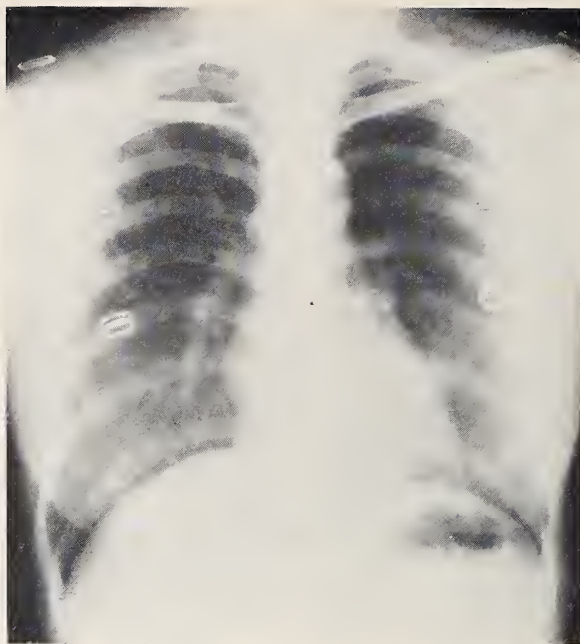


Figure 1.—Minifilm of chest—(three months before onset of illness).

reared in Japan and had always been well until, with her family, she moved to China at age 18. There she had an illness characterized by cough and the expectoration of purulent sputum. Without x-ray examination the condition was diagnosed as bronchitis. It responded slowly to symptomatic treatment over a number of months.

The patient returned to Japan and there married a man serving in the United States Armed Forces. He brought her to this country, where, speaking little English, she had difficulty in adjusting to her new surroundings. The difficulty was soon enhanced by her becoming pregnant. About four months before the onset of the present illness she had normal delivery of a boy baby. A minifilm of the chest at that time (Figure 1) was interpreted as normal, as were the results of routine laboratory studies done at that time.

The patient was small and healthy appearing. Oral temperature was 98.4°F. Physical examination, including the nervous system, demonstrated no abnormalities.

Results of routine laboratory work were within normal limits, except for an elevated sedimentation rate (Table 1). Before the report was received on the sedimentation rate, diazepam (Valium®) was prescribed on the presumption that the complaints were functional in nature. No relief was obtained, however, and when the sedimentation rate was found to be accelerated the patient



TABLE 1.—*Spinal Fluid Studies (1962-1964)*

	23 Aug. 1962	24 Aug. 1962	3 Sept. 1962	21 Sept. 1962	3 Oct. 1962	19 Oct. 1962	19 Feb. 1963	20 Aug. 1964
1. <i>Appearance</i> .....	Colorless	Colorless	—	—	Colorless	—	Colorless	Colorless
2. <i>Pandy</i> .....	Increased	Same	—	—	Same	Negative	—	Negative
3. <i>Cells (cu mm)</i> .....								
(a) Erythrocytes.....	81	10	—	0	3	0	0	410
(b) Leukocytes.....	103	180	258	121	10	9	3	3
% Polymorphonuclears..	6	11	—	0	—	0	—	—
% Mononuclear cells*	94	89	—	100	—	100	—	—
4. <i>Kohner</i> .....	Negative	—	—	—	—	—	Negative	Negative
5. <i>Colloidal Gold</i> .....	4433210000	—	—	5543211000	—	1111000000	0111000000	1221000000
6. <i>Protein</i> .....								
(mg per 100 ml).....	56	63	122	41	27	23	14	13
7. <i>Glucose</i> .....								
(mg per 100 ml).....	—	39	19	37	40	72	85	74
8. <i>Chlorides</i> .....								
(mEq/L).....	—	115	—	110	120	110	130	115
9. <i>Sediment</i> .....								
(a) Gram Stain.....	No Organisms	Same	—	—	—	—	—	No Organisms
(b) Acid Fast Stain.....	No Organisms	Same	—	—	—	—	—	No Organisms
(c) India Ink Mount.....	—	—	—	Cryptococci noted	Cryptococcus (degenerative forms) noted	—	—	No Organisms
10. <i>Cultures</i> .....	Acid Fast bacilli not seen	Acid Fast and fungi not seen	—	—	Cryptococcus	Negative for Cryptococcus	Same	Same
11. <i>Miscellaneous</i> .....	Guinea pig inoculation negative	Same—no Pellicle on standing 24 hours	Complement fixation cocci-diodomycosis-negative	1/3 of mononuclear forms are identified as Cryptococci (viable and degenerative forms)	—	No Organisms	Same	Same

\*On reviewing these slides at a later date many of the cells reported as Mononuclear cells are noted to be organisms (Cryptococci).  
—Determination had not been requested.

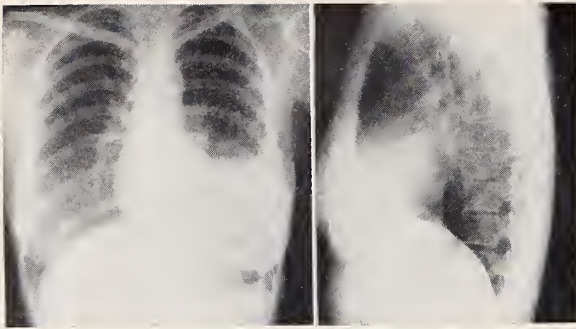


Figure 2.—Posterior-anterior and lateral views of chest 22 August 1962 (several weeks after onset of illness) demonstrating consolidation of lingular portion of left upper lobe.

was put in hospital on 22 August 1965. On physical examination there, the only abnormality noted was slight nuchal rigidity.

The investigation then carried out included:

- X-ray examination of the chest on the day of admission that demonstrated an area of consolidation in the lingular portion of the left upper lobe consistent with pneumonia (Figure 2). Films of the skull were reported as normal.
- An electroencephalogram, reported as normal.
- Numerous spinal fluid examinations (Table 1), never showing increased pressures, but in other respects decidedly abnormal at first, then gradually becoming less so.
- Intracutaneous tests for coccidioidomycosis and tuberculosis with purified protein derivative No. 1, with results negative.
- A diagnostic thoracentesis, from which no fluid was obtained and that resulted in pneumothorax.
- Laboratory studies (Table 2) showing progressive anemia, increasing sedimentation rates, slight elevation of some serum urea nitrogen determinations, hypokalemia on occasions, urine normal except for the presence of organisms, and sputum showing the presence of organisms on direct smear and culture on many occasions.

Other laboratory studies not included in Table 2, all with normal results, included blood viral studies, lupus erythematosus preparation, and complement fixation tests for coccidioidomycosis on blood and spinal fluid. Abnormal results included an anti-streptolysin titer of 300 Todd units, electrophoresis of serum proteins demonstrating decreased albumin and elevated alpha<sup>1</sup> beta and gamma globulins, a cephalin flocculation reaction

of 3+ in 48 hours and a bromsulphthalein test showing dye retention of 11 per cent in 45 minutes. A number of these findings suggested the possibility of impaired liver function.

## Therapy

During the period in hospital, five units of blood were administered and care otherwise was of three categories:

1. *With a presumptive diagnosis* of pneumonia with meningeal involvement thought to be non-specific initially and later tuberculous 22 August to 28 August, penicillin, sulfadiazine and tetracycline hydrochloride were given with the later addition of streptomycin and iso-nicotinic hydrazide-INH.
2. *On detection of spherules* in the sputum, at first thought to represent coccidioidomycosis, the therapy already outlined was discontinued and the administration of amphotericin B was begun. Cultural media subsequently demonstrated the presence of colonies that were luxuriant and glistening in appearance—in contrast to the sparse growth of dry and powdery type colonies characteristic of coccidioidomycosis. India ink preparations microscopically demonstrated thick-walled budding forms consistent with *cryptococcus neoformans*.<sup>\*</sup> Amphotericin B therapy was begun with the intravenous administration of 5 mg in 1,000 ml of 5 per cent glucose in water and progressively increased (daily or every other day) by increments of 5 mg (or more) until ultimately a total of 50 mg was being administered on the days of therapy. The administration of 50 mg in 1,000 ml of glucose in water at first (and then in 500 ml) was carried out daily for the most part. Often the fluid was infused in as short a period as three hours, although sometimes the period was extended to as much as 16 hours. Depending largely upon the patient's reaction, when the reaction was particularly severe: (a) therapy was stopped for a day or more, and (b) the amphotericin infusion was repeatedly interrupted by the substitution of appropriate fluids and electrolytes; then, as the reaction subsided, the amphotericin would be resumed, resulting in the prolongations. The distressing symptoms attending the administration were somewhat ameliorated by the use of sedation and anti-nauseants. Ultimately a total of 1,600 mg of amphotericin B was administered intravenously.

<sup>\*</sup>Confirmed by the Department of Microbiology, Los Angeles County General Hospital.



TABLE 2.—Results of Laboratory Studies (1962-1964) Not Including Spinal Fluid (see Table 1) etc\*

	Before Hospital Admission (interval 4 days)	During Hospitalization (interval 11 weeks)		Following Hospital Discharge (interval 22 weeks)
		First week	2nd through 11th week	
1. <i>BLOOD</i>				
(a) Hemoglobin (gm/100 ml).....	12.1	12.6, 10.6	9 determinations range: 7.0 (post operatively) to 12.4	7 determinations range: 9.8 to 12.6
(b) Sedimentation Rate (mm/hr)...	89	16	3 determinations range: 7 to 30	8 determinations range: 1 to 50
(c) Serum Proteins (mg/100ml)....	—	7.5	7.8	6.5
Albumin.....	—	3.3	5.3 4th week	3.5
Globulin.....	—	4.2	2.5	3.0
(d) Electrolytes (mEq/L)				
Urea Nitrogen.....	—	13	9 determinations range: 7 to 33	—
Potassium.....	—	4.5	5 determinations range: 3.1 to 3.7	—
CO <sub>2</sub> C.P. ....	—	26.4	—	—
Chlorides.....	—	100	105 10/10/64	—
Sodium.....	—	120	134 day of surgery	—
(e) Cultures.....	—	3 Negative	—	—
2. <i>URINE</i>				
(a) Routine.....	3 to 4 WBC's	3 to 4 WBC's	4 examinations all showing occ. WBC and RBC's	3 to 4 WBC's
(b) Direct Smear.....	—	No Organisms seen	Cryptococci noted in 5th week	No Organisms seen
(c) Cultures.....	—	No Growth	Moderate growth Streptococci	Negative
3. <i>SPUTUM</i>				
(a) Direct Smear.....	—	2 specimens—one showed double walled cells	3 specimens. Last, on day prior to surgery. All showed Cryptococci	1 specimen No Organisms
(b) Culture.....	—	Cryptococcus neoformans	Culture prior to day of surgery. Negative	Negative
*Miscellaneous tests—refer to text. —Determination had not been requested.				

\*Miscellaneous tests—refer to text.

—Determination had not been requested.

During the course of therapy it was noted that: (a) the administration of the material every day seemed preferable, in that it was the opinion of many observers that the systemic reactions were less severe than when periods of a rest of a day or more intervened without therapy; (b) phlebitis, which has been referred to consequent to the administration of amphotericin,<sup>1,7,12</sup> was not encountered; (c) the symptoms associated with the administration of amphotericin gradually became more intense, due either to its continued administration or possibly to progression of the disease, suggesting limitation of continued use.

3. *Excision* of the pulmonary lesion was considered because of the unchanging radiological appearance of the chest lesion, the continued presence of organisms in the sputum and the supposition of eventual limitation of amphotericin ther-

apy. At the juncture when the spinal fluid findings were minimal, lingulectomy, together with the removal of parabronchial lymph nodes, was carried out. Postoperative therapy with amphotericin had been contemplated; but with doses of as little as 5 mg intense reactions were again encountered, and when a total of only 100 mg had been administered, therapy was discontinued. This eventuality was particularly disturbing in view of the presence of organisms in the sputum immediately before operation and later the demonstration of innumerable organisms in the surgical specimen.

### Clinical Course

The progress of the patient during the time in hospital might be considered in two phases:

(1) *Before the administration of amphotericin* when the patient's symptoms of headache, nausea,

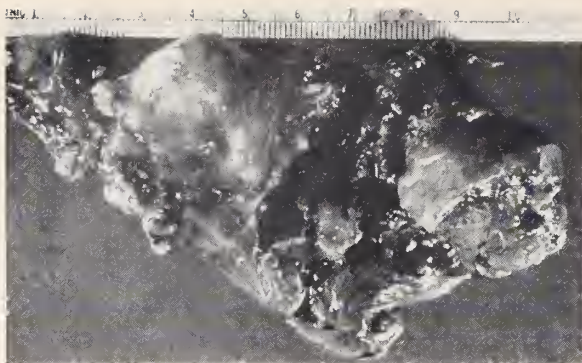


Figure 3.—Photograph of surgical specimen (lingular portion of left upper lobe).

vomiting and anorexia became progressively worse, and were accompanied by increasing fever (ultimately to 105°F).

(2) *After the beginning of amphotericin therapy*, except for the systemic reactions accompanying its administration, the patient's symptoms gradually tended to regress to the point that she was occasionally released for several hours or even a day or two to visit at home.

The illness resulted in a weight loss of 10 pounds which the patient was slowly regaining at the time of her release from the hospital on 30 October 1962.

### Pathological Report

The surgical specimen (Figure 3), which included the lingula of the left upper lobe of lung, measured 8×5.5×5.0 cm. Sections (Figure 4) showed a discrete but non-encapsulated subpleural ovoid lesion surrounded peripherally by numerous discrete or confluent satellite nodular areas. These all showed greyish, mucoid-appearing cut surfaces. Microscopic examination of both the pulmonary lesion and the parabranchial lymph nodes showed obliteration of the normal structure by an extensive granulomatous reaction with an abundant population of organisms morphologically consistent with *cryptococcus neoformans*. Many cryptococci were readily demonstrable within the lumina of a number of bronchioles passing through the pulmonary granuloma.

### After Release from Hospital

The patient was seen at regular intervals after she was released from hospital. In addition to clinical evaluation, x-ray examinations of the chest and certain laboratory studies were carried out (Table 2). The patient expressed increasing con-

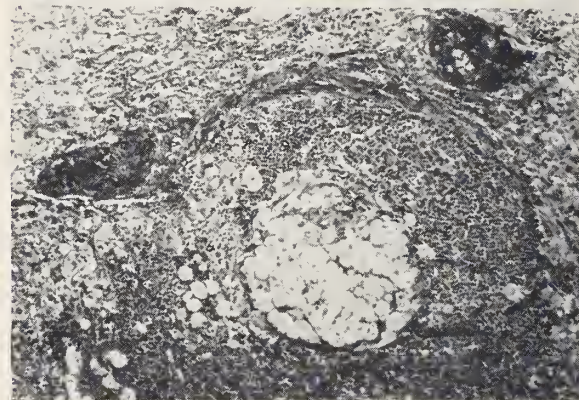
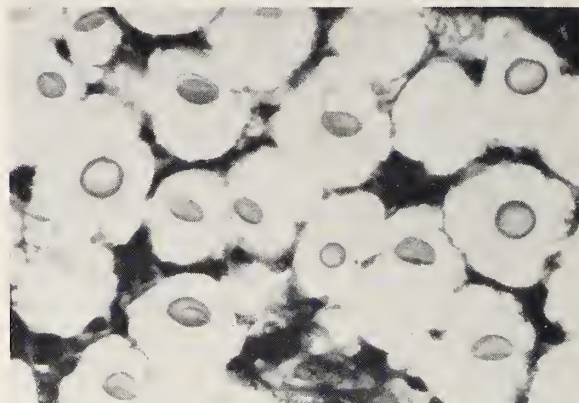
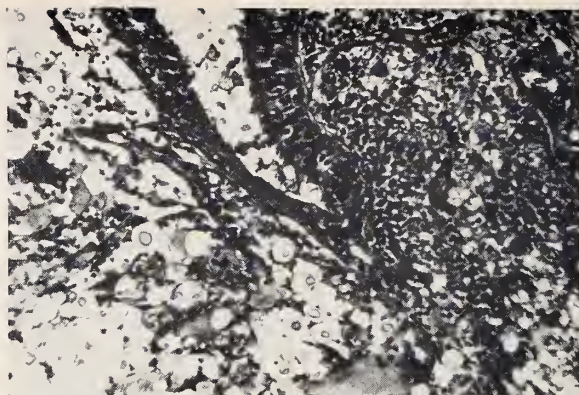


Figure 4.—Sections of surgical specimen. *Upper*—lung, a portion of bronchiole showing "rupture" of cryptococcal granuloma with extrusion of organisms into lumen (×100). *Middle*—lung, showing density of distribution of organisms despite preceding administration of amphotericin, 1,600 mg (×430). *Lower*—(left parabranchial) lymph node showing virtually complete obliteration of nodal architecture by granulomatous reaction. Innumerable cryptococci, some replacing germinal center of node (×100).

cern about a gradual increase in weight, insomnia and marital difficulties. Continued complaints of this type resulted in a conference of both the husband and the wife with the physician, at which the advisability of appropriate consultation was suggested.



On 20 August 1964, two years after the first admission to the hospital, the patient's history was again reviewed with her, and physical examination was carried out. The body weight was exactly the same as it had been two years earlier. On the skin of the lower eyelids there were several 2 to 3 cm raised white lesions, thought to be milia, that had not been there before. Otherwise, nothing of note.

Investigation including x-ray films (Figure 5) and laboratory work was carried out. Laboratory determinations other than those recorded in Table 2 were as follows:

(1) *Those within normal limits*—fasting and two-hour postprandial blood sugar, serum calcium phosphorus and alkaline phosphatase, serum transaminases (SGOT and SGPT) and serum proteins.

(2) *Abnormal*—Bromsulphthalein retention of 10 per cent in 45 minutes, thymol turbidity of 9.5 units, cephalin flocculation of 4+ in 24 hours, and a slight decrease in albumin on electrophoresis of the serum proteins. A tuberculin test (Tine-Ledcrle) was interpreted as negative.

In summary, the laboratory determinations continued to indicate some degree of anemia and impairment of liver function.

When the patient was last examined, except for abnormal results of laboratory tests, of unknown cause, there was no clinical evidence of recrudescence of the disease.

## Discussion

The illness of the patient at age 15, diagnosed as bronchitis, might theoretically be considered as having been a localized form of cryptococcosis with apparent spontaneous recovery or remission. This possibility seems unlikely, however, in view of the lack of radiological evidence of a former infection (areas of scarring or fibrosis); x-ray examination of the chest showed no abnormality three months before the onset of the present illness.

The presumption that the disease was of recent onset might suggest that it was contracted locally. If so, questions that arise are: Is it endemic in this area, and is it possible that the disease occurs but is not being recognized clinically?

In the present case there were features consistent with precipitating causes of the disease that have been reported in the literature—the upper respiratory tract infection that was treated with broad spectrum antibiotics, following pregnancy



Figure 5.—Posterior-anterior and lateral views of chest 20 August 1964 (two years after onset of illness) demonstrating residual effects of thoracotomy; otherwise normal.

which might have produced some degree of debility.

The psychological problems evident before the onset of the illness were again manifested in increasing degree as the interval of remission lengthened.

The early request for spinal fluid examination specifically for torulosis in the present case was owing to a coincidence: The author had attended a conference on torulosis shortly before seeing this patient. Even so, it was only by fortuitous observations of the personnel of the pathology department that the etiological agent was identified. In retrospect the variety of diagnoses and treatment in the nine days preceding the correct diagnosis may seem to have been unwarranted.

The intravenous administration of amphotericin in the dosage given (preoperatively 1,600 mg) reduced the number of organisms in the sputum but did not affect the radiological appearance of the chest lesion. Also the spinal fluid contents became almost normal and the lesion in the chest was therefore considered the "focus" of infection. For this reason amphotericin was not administered intrathecally.

Boeck's sarcoid might be considered in the differential diagnosis of cryptococcosis, in light of the initial skin manifestations, the altered serum proteins, the abnormal liver function tests, the negative tuberculin tests and finally the presence of parabranchial adenopathy. Hilar adenopathy is possibly more consistent with sarcoidosis but is rarely encountered in pulmonary cryptococcosis,<sup>7</sup> although three cases with this finding were reported in 1958.<sup>11</sup> It is conceivable that the location of the pulmonary lesion, particularly if it were more centrally placed, could result in hilar involvement in view of the massive parabranchial

lymph node involvement that was encountered in the present case.

Evidence of impairment of liver function was noted during the course of treatment and was still evident on the final evaluation 22 months after treatment. Possible causes that warrant consideration are involvement of the liver as a further manifestation of dissemination of cryptococcosis, co-existing sarcoidosis or other diseases and toxic effect that might have resulted from the administration of amphotericin B in relatively large doses to a patient of less than usual weight. Biopsy of the liver in the present case has been considered but not carried out.

The nature of this disease and its apparent ability to exist in a state of remission suggest that it may take months or even years of observation to establish the eventual outcome in the present case and in others of similar nature. A more optimistic viewpoint might be justified based on the time interval in which relapses occur; in this regard it has been reported this complication is most likely to occur in the 12 months following therapy.<sup>13</sup> The term *cured* should be used with caution, *remission* perhaps being a better one in the circumstances.

## Summary

A case of cryptococcosis of the disseminated variety involving the nervous system, the lungs and possibly the liver and kidneys has been reported. Therapy included preoperative and postoperative administration of amphotericin B intravenously, and excision of the pulmonary lesion. Up to the time the patient was last observed, more than three years after operation, there had been no recurrence of symptoms.

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## Syndrome of Cyanosis, Symmetry and Splenic Agenesis

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SINCE NOT ALL SYNDROMES of congenital heart disease with other systemic malformations can be surgically corrected, it would be helpful to identify them as early as possible in the newborn period.

More than a hundred cases of a syndrome characterized by cyanotic heart disease, absence of the spleen and a remarkable tendency toward symmetry of all paired organs have been reported.<sup>1-6</sup> More than 90 per cent of affected infants die before the age of two months. The condition is identifiable ante-mortem by examination of a smear of peripheral blood and an abdominal x-ray film.

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Submitted 22 July 1965.



Consequently, differentiation of this anomaly from other cyanotic cardiac abnormalities that have a better prognosis is now possible.

It is the purpose of this paper to call attention to this syndrome with a case report and to discuss the identification of the condition.

### Report of a Case

A 10-day-old Mexican boy was admitted to the Fresno County General Hospital 11 January 1965 because of increasing irritability and respiratory distress. At birth he weighed 10 pounds 1 ounce; the Apgar score was 9. When the baby was 36 hours old, one observer noted minimal subcostal retractions and questionable cyanosis while the baby was crying and feeding. An x-ray film showed a mass in the upper lobe of the left lung. This was thought to be thymic tissue. The following day the baby appeared improved and was discharged. At home, his respirations were believed abnormally rapid. Otherwise all seemed satisfactory until the day before the present admission.

The mother (gravida IV para IV) had delivered infants weighing 8 pounds 14 ounces, 8 pounds 6 ounces, and 7 pounds 11 ounces. Mild preeclampsia developed in each of the previous pregnancies. In light of the large size of the new baby, she was to return in six weeks for a diabetic evaluation.

At the time the infant was readmitted, he was mildly cyanotic, the heart rate was 176, respirations 88, temperature 100°F, weight 10 pounds 6 ounces, and blood pressure was 100 by flush. A grade II systolic precordial murmur was noted. Penicillin and kanamycin sulfate were started in the belief that the mass in the left upper lobe was caused by pneumonitis. The cardiac shadow was not enlarged. Results of blood chemical determinations were: glucose 84 mg, urea nitrogen, 12.5 mg, calcium 10.1 mg, and phosphorus 8.3 mg per 100 ml; sodium 134 mEq and potassium 4.7 mEq per liter; and carbon dioxide 21 volumes per cent. Leukocytes numbered 16,100 per cu mm with a normal differential and packed cell volume was 45.5 per cent. Later the packed cell volume was 54 per cent and the hemoglobin 16.2 gm per 100 ml. Alpha streptococci were isolated on a throat culture and coagulase-positive staphylococcus aureus on a nasal culture.

On the fifth day in hospital, the patient being unimproved the case was reviewed. Clinically

right heart failure was present. Mild cyanosis at rest was apparent. An electrocardiogram was interpreted as showing severe right axis deviation and right ventricular and probably right atrial hypertrophy. Cardiac fluoroscopy showed no appreciable heart enlargement. A homogenous shadow was seen in the left upper lung field (Figure 1). Pulmonary vascularity was slightly increased. The barium filled stomach lay to the right of the vertebral column with the greater curvature forming the right border (Figure 2). The left pulmonary artery was not clearly visible.

A diagnosis of probable total anomalous pulmonary venous return was made. Administration of digoxin, Lonalac, increased oxygen and mercurial diuretics was begun and the patient was placed in an infant seat. When further deterioration developed, intermittent positive pressure breathing was started. On the eleventh day in hospital the patient, then three weeks old, died.

The following conditions were observed at autopsy:

- Persistent truncus arteriosus with a common pulmonary artery arising from the descending thoracic aorta and quickly dividing into right and left branches.
- Single ventricle and single atrium with common AV canal.
- Total anomalous pulmonary venous drainage into the right side of the common atrium.
- Three-lobed left lung as well as right with atelectasis of the left upper lobe.
- Large left lobe, giving a symmetrical appearance to the liver.
- Absence of the spleen.
- Mid-line position of the stomach.

### Comment

Ivemark<sup>1</sup> designated this combination of abnormalities as "asplenia, a teratologic syndrome of visceral symmetry." His excellent review of 69 cases indicated that both an anomalous atrio-ventricular canal and cono-truncus occur with asplenia in almost all cases. Total anomalous venous return, dextrocardia and cor biloculare, together with other systemic and pulmonary venous malformations, are other severe and frequent cardiac findings. The tendency toward bilateral symmetry is invariably present in all paired organs. Unpaired organs such as the gallbladder, the

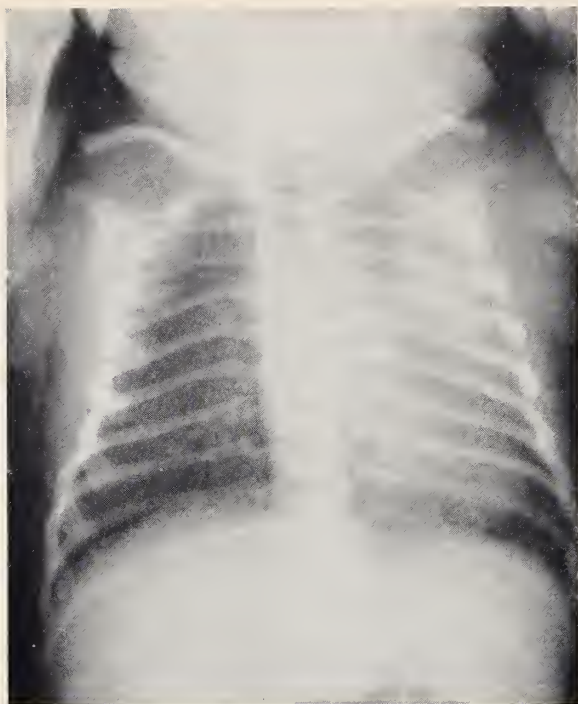


Figure 1.—Film of chest shows a left subdiaphragmatic mass representing the symmetrical left lobe of the liver. Additionally there is the upturned apex of right heart enlargement, overcirculation of the lungs and atelectasis of the upper left lobe.

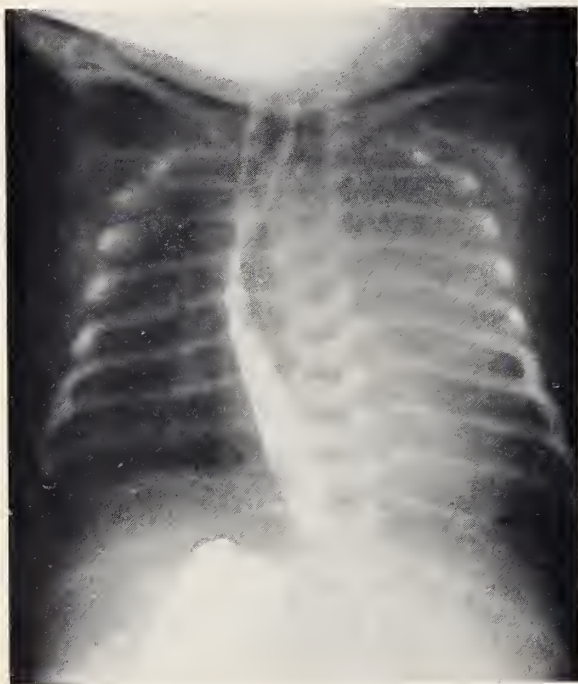


Figure 2.—Esophagram showing displacement to right by enlarged common atrium. Note medial position of stomach with rotation caused by enlarged left lobe of liver.

stomach and pancreas assume a mid-line position. Notably the left lobe of the liver mirrors the size of the right. Both lungs usually have three, less frequently four, distinct lobes. Commonly there are two superior vena cavae, common atria and ventricles and a common mesentery.

Theoretically, any number of agents could cause the syndrome by arresting development at a critical stage. Agenesis of the spleen is a constant factor. The splenic primordia develop from the dorsal mesogastrium approximately 31 days following ovulation. Subsequently the gelatinous reticulum formed from the cardiac jelly ultimately partitions the cono-truncus and also condenses into the atrio-ventricular cushion. The atrioventricular canal is divided at about 34 weeks; two weeks later the division of the cono-truncus is completed. Later the aortic and pulmonary valves are formed, followed by the mitral and tricuspid.<sup>1</sup>

Putschar and Manion<sup>4</sup> expressed belief that the syndrome is a suppression of laterality associated with agenesis of the spleen. Thus the symmetry of paired organs and the mid-line placement of single viscera can be considered a variant of situs inversus. The spleen is in fact the only unilateral mesenchymal organ in the body.<sup>2,3</sup>

Cono-truncus maldevelopment creates sequential anomalies; most primitive is a truncus arteriosus followed successively by pulmonary atresia, pulmonary stenosis and transposition without stenosis.

Apart from this syndrome, congenital asplenia is rare. Absence of the spleen in an infant with congenital heart disease is prognostic of early death. In only four of 80 cases reviewed by Lyons were the patients alive at three years of age. Cardiac catheterization and angiocardiology are inadvisable; apparently they hasten death. Shunt procedures have not been rewarding; typically a septal defect with or without patent ductus already is present.<sup>2</sup>

Diagnosis can be made ante mortem. In 1952 Willie and Gasser<sup>7</sup> described cytologic features of a smear of peripheral blood that are pathognomonic of asplenia. The presence of Howell-Jolly and Heinz bodies in the red blood cells, together with polycythemia, siderocytes, target cells and normoblasts, is characteristic. An ordinary Wright stain is sufficient to identify Howell-Jolly bodies, but special staining is required for identification of Heinz bodies. Hepatic symmetry visualization of



the gastric bubble at the midline or on the right side are supporting evidence.

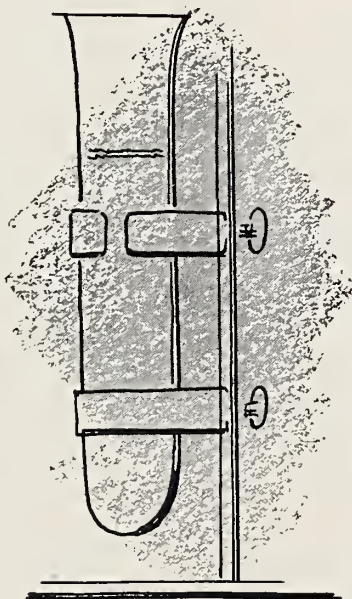
### Summary

A case of a syndrome of cyanotic congenital heart disease, symmetry of the internal viscera and splenic agenesis is presented. Over 100 cases have been reported in the literature. Asplenia is a common factor. The condition is essentially not amenable to surgical repair and is invariably fatal in early infancy. Ante mortem diagnosis can be obtained with a blood smear and a plain film of the abdomen, thus distinguishing this syndrome from cardiac anomalies for which the prognosis is better.

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# Medical Staff Conference

## Presentation of Two Cases

### 1. Disorders of Bilirubin Metabolism

### 2. Sclerosing Cholangitis

*These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. They are prepared from transcriptions by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Professor of Medicine and Chairman of the Department of Medicine.*

## Disorders of Bilirubin Metabolism

DR. A. MARVIN BROOKS:\* The patient is a 26-year-old student who was admitted to the University of California Medical Center because of hyperbilirubinemia. Three months before admission, recurrent headaches developed, associated with malaise and mild fever. The patient had noted no jaundice, itching, vomiting, nausea or change in the color of urine or stools. There was no history of recent drug ingestion or of exposure to hepatotoxic agents. He had had a "flu" injection about three months before admission. At about the time the patient began to have the previously mentioned symptoms, infectious mononucleosis was diagnosed in his roommate.

Ten years before the present admission, the patient had had a protracted bout of hepatitis which was characterized by jaundice and vomiting. There had been no recurrence of these symptoms since that time. A brother, with whom he had recently been in contact, was in hospital with severe intrahepatic cholestatic jaundice of unknown cause at the time the patient was admitted.

On physical examination slight splenomegaly was noted. A complete blood cell count was within normal limits. The hematocrit was 48 per cent. A representative bilirubin was: Total, 3.1 mg per 100 ml, only 0.2 mg conjugated. Glutamic oxaloacetic transaminase (SGOT), glutamic pyruvic transaminase (SGPT) and lactic dehydrogenase (LDH)

were all within normal limits. Basic phosphatase was 5 Bodansky units. Heterophile agglutination was not elevated. No abnormalities were noted on biopsy of a liver specimen obtained percutaneously. A prussian blue stain of this specimen showed no stainable iron. The reticulocyte count was 3.9 to 5.4 per 100 ml. The serum haptoglobin level was within normal limits and results of direct and indirect Coombs tests were negative.

The red cells in the blood were slightly macrocytic and a few spherocytes were seen. The hemoglobin electrophoresis was normal. The osmotic fragility of the red cells was slightly increased. Bone marrow aspirate showed pronounced erythrocytic hyperplasia. Assay of the red blood cell glucose-6-phosphate dehydrogenase was within normal limits. The survival of Cr<sup>51</sup> tagged red blood cells was 17.5 days. The ratio of Cr<sup>51</sup> uptake in the spleen to the liver was slightly increased, 2.6 to 1, the normal being 2.0 to 1. Two 72-hour stool collections contained decidedly elevated amounts of urobilinogen—5.4 gm and 2.3 gm per 24 hours. Urobilinogen in a 24-hour urine collection was within normal limits—1.3 mg. The patient was discharged with a diagnosis of hyperbilirubinemia secondary to spherocytosis and possibly to a bilirubin shunt from sources other than circulating red blood cells. (The patient was brought in.)

DR. LLOYD H. SMITH, JR.:† We appreciate your coming in for this exercise today. How are you feeling?

\*Resident in Medicine.

†Professor of Medicine and Chairman of the Department of Medicine.



*Patient:* I feel as I did before. I have a constant mild headache. At times it becomes worse and makes me more irritable and nervous.

*Dr. Smith:* Do you have any abdominal pain?

*Patient:* No.

*Dr. Smith:* Any itching?

*Patient:* No.

*Dr. Smith:* Have you noticed any yellowness of your eyes?

*Patient:* No, I haven't.

(Patient leaves.)

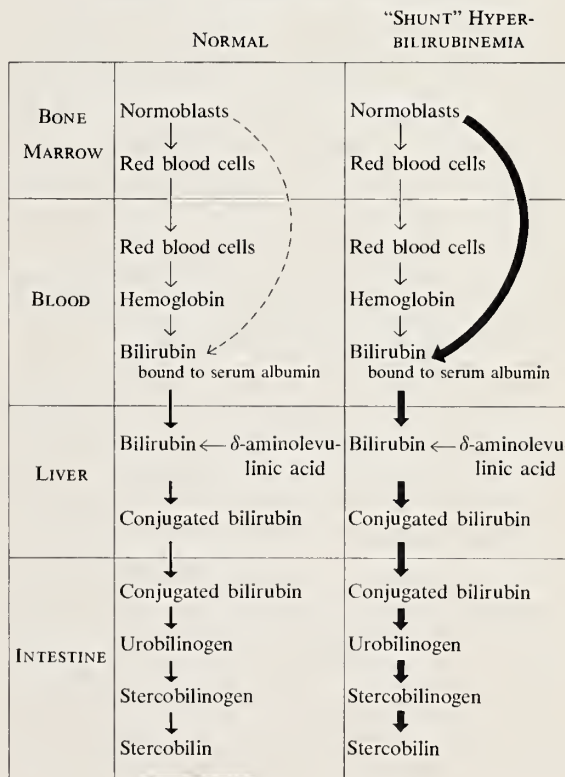
*Dr. Smith:* Our speaker today, Dr. Rudi Schmid, was graduated from the University of Zurich, Lausanne, and Geneva. From this poly-academic beginning, he has subsequently been associated with the University of Minnesota, Columbia University, National Institutes of Health, Harvard University, and now the University of Chicago, where he is currently professor of medicine. Although he has been productively interested in many metabolic disorders over the years, his most central theme throughout these peregrinations has been the study of pyrole metabolism. This has been true for both abnormalities in the synthetic pathway since he is certainly one of the leading authorities in the world on porphyria. Recently he has been carrying out studies on the degradation and excretion of pyroles and tetrapyroles, particularly bilirubin metabolism. We are delighted to welcome him here today to discuss this interesting patient and perhaps to comment more generally about his studies on bilirubin metabolism.

DR. SCHMID: Our patient today presents a number of interesting features which we would like to explain in pathophysiologic terms. Obviously he has chronic, unconjugated hyperbilirubinemia with overproduction of bile pigment; this is evident from the large increase in fecal urobilinogen. Fecal urobilinogen does not measure the exact amount of hemoglobin which is broken down, but values as large as those in this patient indicate that hemoglobin turnover must be greatly accelerated. Yet, there is little evidence of significant hemolytic anemia. Hemoglobin and hematocrit are normal, reticulocytosis is slight and red cell life span is only moderately shortened. From the hematologic findings in the blood one would predict a slight overproduction of bilirubin, but the fecal urobilinogen suggests a much larger load of bile pigment. It obviously doesn't add up, and this is what Dr. L. G. Israels, and his coworkers have called

"shunt" hyperbilirubinemia. I believe that this is an infrequent yet important cause of jaundice, but I do not like the term "shunt" because it implies a metabolic shunt, such as is present in primary gout. This is not the case here; rather we are dealing with accelerated formation and breakdown of erythroid cells, in part in the circulation, and to a much larger extent in the bone marrow (ineffective erythropoiesis).

Before we go on, let us look at some general aspects of bile pigment metabolism. When hemoglobin of senescent red cells is degraded, its protoporphyrin ring is converted to a straight tetrapyrrole, the basic structure of all bile pigments. The major pigment formed is bilirubin, which in the plasma is bound to albumin and carried to the liver. Here, three metabolic steps can be distinguished. First, uptake of bilirubin by the liver cells: This involves detachment from the plasma albumin complex, transfer of the pigment molecule across the cell membrane, and subsequently, reattachment to an intra-cellular carrier. Second, conjugation of bilirubin by the microsomal enzyme glucuronyl transferase, which attaches two glucuronic acid molecules to the pigment. And, third,

#### SUMMARY OF BILIRUBIN METABOLISM



secretion of conjugated bilirubin into the bile, which appears to be an "active," energy-requiring mechanism. The last step is probably the rate-limiting factor in the overall transport of bilirubin from the plasma to the bile. Defects in this secretory mechanism result in impaired excretion of bilirubin glucuronide with consequent accumulation of conjugated pigment in the plasma. Examples are the Dubin-Johnson syndrome and drug-induced cholestasis. In our patient this obviously is not the case, since he has *unconjugated* hyperbilirubinemia, and we have to look for another explanation.

The disturbance evidently lies in a disproportion between the quantity of unconjugated bilirubin presented to the liver and the maximal rate at which the liver can either take up the pigment or conjugate it. Examples of the effect of defective conjugation are the Crigler-Najjar syndrome and the Gunn rat, both of which are associated with severe life-long unconjugated hyperbilirubinemia. Impaired hepatic uptake is believed to be the cause of the mild jaundice in Gilbert's disease or constitutional hepatic dysfunction, and of a similar type of icterus in a mutant Southdown sheep, which Dr. Charles Cornelius of the U. C. Davis campus is studying. In all of these forms of unconjugated hyperbilirubinemia, fecal urobilinogen excretion is either normal or decreased, because the bilirubin load is normal and the principal defect involves hepatic removal of the pigment from the plasma. Since, in our patient, fecal urobilinogen was greatly increased, his primary abnormality must consist of a bilirubin *overload* which exceeds the liver's capacity to handle the pigment. Since this overload does not appear to be accounted for by a comparable degree of hemolysis in the peripheral blood, we have to look for another source from which the bilirubin could be derived.

Many of you are familiar with the classic studies on the origin of bile pigments which were published in 1950 by Gray and Neuberger in London, and by London, Shemin and Rittenberg in New York. These studies showed that in normal persons approximately 85 per cent of all excreted bile pigment is derived from hemoglobin of senescent red cells destroyed at the end of their life-span. However, a second, smaller bile pigment fraction apparently is derived from other sources. In investigations with labeled precursors it was found that approximately 15 per cent of the excreted labeled bile pigment appeared in the stool within

the first eight to twelve days after isotope administration. Obviously, this so-called early labeled stercobilin could not have been derived from destruction of mature labeled red cells because, at the time of its appearance in the stool, labeled young erythrocytes were still being released into the circulation. The origin of the early-labeled bile pigment was obscure, but various possibilities were considered, including derivation from heme formed in excess of globin, overproduction of hemoglobin in maturing erythroid cells, destruction of a few maturing red cells in the bone marrow, or formation from a pathway not involving hemoglobin. Marcel Bessis in Paris has suggested the intriguing possibility that early-labeled bile pigment may be derived from small amounts of hemoglobin which are liberated in the course of enucleation of the normoblast. While it was difficult to decide which of these several possibilities was correct, most investigators agreed that the early-labeled stercobilin probably originated in the course of red cell formation and hemoglobin synthesis in the bone marrow.

In the past few years, however, several observations have been reported which cast some doubt on this concept. Despite serious methodologic difficulties, isotopic studies yielded results which, from a kinetic standpoint, were difficult to reconcile with an erythropoietic origin of the early-labeled bile pigment fraction. A year ago, Dr. Stephen Robinson searched for a suitable experimental model for the study of bile pigment formation which would overcome the methodologic limitations inherent in previous investigations. It turned out that the best model was the Gunn rat, which is a mutant Wistar rat with a hereditary defect in bilirubin glucuronide formation and a consequent life-long unconjugated hyperbilirubinemia. In these animals, tracer techniques were used to determine the half-life, turnover and miscible pool of bilirubin. Based on these data and with the use of a digital computer, the rate and magnitude of isotope incorporation into bilirubin could be calculated from the specific activity of the pigment in the plasma. This model permitted studies over unlimited periods of time in intact animals under physiologic conditions. Dr. Robinson found that approximately 85 per cent of the labeled bilirubin is formed during a period 40 to 70 days after isotope administration, which corresponds to the average life-span of rat erythrocytes of approximately 60 days. In addition, approximately 15 per cent of the labeled bilirubin appeared as early-labeled pigment.



The surprising finding was that this early-labeled pigment appeared very early indeed: The highest rate of pigment formation occurred during the first two hours, and the process was almost completed within 12 hours. This very rapid formation of early-labeled bile pigment did not appear to be consistent with the concept that this fraction could be derived from labeled hemoglobin in the bone marrow. The kinetic data suggested another source and, like other investigators, we suspected the liver. This suspicion was reinforced by the observation that in hypertransfused rats where erythropoiesis is suppressed, the kinetics and magnitude of the early-labeled pigment fraction remained unaltered.

The hepatic origin of this pigment fraction was finally established by experiments with isolated, perfused rat liver. In these studies it was shown that the liver forms bilirubin from labeled glycine or  $\delta$ -aminolevulinic acid at a rate which corresponds to the early labeled fraction in intact normal animals. The mechanism by which this occurs in the liver is unknown, but it most likely involves a hepatic heme fraction with a very rapid turnover. Thus in rats, and probably in normal man, the early-labeled bile pigment fraction largely represents pigment that is derived from the liver and has little to do with erythropoiesis in the bone marrow. It is tempting to speculate that in some forms of liver disease, hepatic bile pigment formation may be increased, thus contributing to development of jaundice, but to date this has not been supported by concrete evidence. Our patient did not show evidence of hepatic dysfunction and it is improbable that the large pigment load was derived from the liver.

The most likely source for the overproduction of bilirubin in this patient is the bone marrow. He had erythroid hyperplasia of the marrow out of all proportion to the relatively slight increase in reticulocytes in the peripheral blood. This is commonly referred to as "ineffective erythropoiesis," implying that a significant fraction of maturing erythrocytes is defective and is destroyed in the marrow before being released into the blood. This is particularly striking in thalassemia, pernicious anemia and erythropoietic porphyria, and it also appears to occur in other forms of inherited red cell defects. In patients with thalassemia minor, as much as 80 per cent of the excreted bile pigment appears to be derived from destruction of immature red cells in the bone marrow, which obviously

represents a very high fetal mortality of these cells. Our patient appears to have a defect in his erythroid apparatus which probably is genetically determined and predisposes his erythrocytes to premature destruction in the marrow. Hence only a relatively small fraction of the total erythropoietic effort of the bone marrow results in delivery of red cells to the circulation, but the cells that do reach the blood have an almost normal life-span. The destruction of so many erythroid cells in the bone marrow leads to a large overproduction of bile pigment which in all probability is the cause of the chronic unconjugated hyperbilirubinemia.

From a therapeutic standpoint there is little that can be done because the defect in the developing red cells is intrinsic and cannot be eliminated. Splenectomy may be of little benefit because survival of red cells in the circulation is not much shortened. There are a few points which may be worth considering in the long-term management of this patient. The increased bone marrow activity requires adequate amounts of folic acid, and if the patient is on a marginal diet, folic acid deficiency may develop, causing depression of erythropoiesis.

In patients with pronounced ineffective erythropoiesis, hemosiderosis is likely to develop; and one ought to be on the lookout for signs of iron overloading and, if necessary, correct it. Because of the accelerated red cell turnover, uric acid production may be increased, and if hyperuricemia occurs it should be treated by appropriate means. Barring these complications, the prognosis appears to be quite good, at least as far as can be judged from the limited experience with disturbances of this type.

In summary, I believe that this patient has a defect of erythroid cells which probably is of genetic nature and leads to pronounced ineffective erythropoiesis. It is probable that the accelerated red cell turnover in the bone marrow results in formation of a large amount of bilirubin which exceeds the rate at which the liver can handle the pigment, and that the discrepancy between the pigment load and the capacity of the liver to transfer bilirubin into the bile is the cause of the chronic unconjugated hyperbilirubinemia.

DR. SMITH: We are fortunate in having time for other comments and questions on this intriguing patient and many of the problems brought up in Dr. Schmid's discussion. We are pleased to have with us Dr. Nathaniel I. Berlin, who is the clinical director of the National Cancer Institute, and who

is also an authority on bilirubin metabolism. Dr. Berlin, would you like to make a comment about this case?

DR. NATHANIEL I. BERLIN: I am not prepared, having come to listen, and I can say very little about this specific condition that Dr. Schmid discussed so magnificently. There are a few impressions obtained from our research that I would like to leave you with. It occurred to us that the way to determine whether the early peak was associated with erythropoiesis or not was to obtain patients in whom erythropoiesis was absent by the usual clinical criteria. This we did. The failure to make red cells was documented by low reticulocyte count, by a failure to incorporate radioactive iron into the red cells and by a very slow clearance of radioiron from the plasma. The patients without red cell formation had a very small early-labeled peak after  $C^{14}$ -glycine administration. Fortunately, we had two patients with chronic lymphatic leukemia who responded to a combination of testosterone and adrenalcortical steroids. They were given a second dose of carbon-labeled glycine during a period of intense erythropoiesis. The early-labeled peak was greatly increased, leading us to believe that at least in man the early-labeled peak is largely associated with erythropoiesis.

In dogs, both Schwartz and Watson in Minnesota and Barrett in my own laboratory studied the conversion of glycine to bile bilirubin. In contradistinction to what appears in normal rats, in the normal dogs there appear to be two components to bile bilirubin  $C^{14}$  content curve. The carbon $^{14}$  labeled activity in the second component appears to peak at about day three to four, approximately when one would anticipate that red cells that had taken up radioactive glycine had reached the end of their life span within the marrow and were beginning to enter the peripheral blood. This is the time when if some of these cells were defective in the sense that they did not survive normally in the marrow they would be catabolized. It is also the time when the nucleus is extruded from the normoblast from the normal red cell. In dogs with phlebotomy, this third to fourth day peak was decidedly increased. Later these dogs were made polycythemic by transfusion and this peak was decreased, indicating this source was related quantitatively to the rate of erythropoiesis. Schwartz in Minnesota and Barrett in Bethesda independently estimated that in the early peak in dogs approximately two-thirds of the isotope was derived from

that part of the peak that occurs from days two to six, which we believe is most directly associated with erythropoiesis. This is about the only comment I would like to make, Dr. Schmid, to what you so beautifully presented to us about bilirubin metabolism in man and rats.

DR. SMITH: We have other persons in the audience who are interested in bilirubin metabolism. One of them is Dr. Gerald Grodsky.

DR. GERALD GRODSKY:\* I am less prepared than Dr. Berlin. We have been very much interested in the area that he discussed in his introduction, namely the three-phase concept of bilirubin transport—uptake, conjugation and secretion. Dr. Schmid mentioned that the rate-limiting step for the transport of bilirubin, in rats at least, is the excretion phase, and I would like to make a few comments about that.

Dr. Schmid would have been more accurate to say secretion is the rate-limiting step with large bilirubin loads but not necessarily the limiting step in most physiological situations. It is true that in experiments where large amounts of bilirubin are injected into an animal, one finds that the final maximal rate-limiting step is secretion. But these are very nonphysiological experiments; in fact probably any experiment in which bilirubin is injected in high concentrations (150 mg per 100 ml) in buffer or albumin must be written off, because distribution of these excesses of bilirubin in tissues is far different from that observed with tracer bilirubin as now used in a few laboratories.

The experiments we have been doing recently involve injecting labeled bilirubin, removing the liver at one-minute intervals, then extracting the pigment from the liver and chromatographically determining whether it is conjugated or free. If the rate-limiting step truly were excretion, one would presume that high levels of conjugated bilirubin would be found in the liver, waiting to be excreted. We find, however, that bilirubin is taken up and concentrated by the liver in the free form, so that the conjugation step—not secretion—is rate-limiting.

DR. SMITH: In the discussion today, and I believe also in Israel's decisions concerning his studies, the conclusion was reached that it was the hematopoietic activity which represented the early shunt contribution to hyperbilirubinemia. The suggestion was made by Israel's—and I think also in your discussion—that there might be hepatic overproduc-

\*Associate Professor of Biochemistry.



tion as a shunt production in some cases of jaundice. Is there any direct evidence for this, or is it just speculation? I might also say that we are intrigued by vague analogies of this shunt mechanism to the early glycine shunt which occurs in purine metabolism. Dr. Fudenberg receives the credit for bringing this diagnosis to the attention of the ward team, first off on looking at the bone marrow and hearing the bare outline of the case. Dr. Fudenberg, would you like to comment about this?

DR. H. HUGH FUDENBERG:† As indicated by Dr. Schmid, pronounced erythroid hyperplasia and decided increase in fecal urobilinogen with normal liver function and no, or only slight, increase in hemolytic rate (mild reticulocytosis, mild shortening of red cell survival time, and normal serum LDH and haptoglobin values) are seen in few, if any, conditions other than the one first described by Israels and termed by him "shunt hyperbilirubinemia." Dr. Berlin has indicated that the name is not the most desirable one because the pigments liberated may come from red cell precursors in the marrow rather than from the liver. Nonetheless, the term *shunt* does imply that the pigment does not come from increased hemolysis of the red blood cells in the peripheral blood.

Perusal of the literature suggests that the cases described by Israels in Canada were complicated by the simultaneous presence of a mild form of hereditary spherocytosis, presumably due to genetic linkage of the two traits. It is in this form that mild hemolysis is present and the form in which spherocytes are seen in the peripheral blood. This was true in the patient presented today. In the patient reported by Klaus and Feine in Germany, spherocytosis was not present and red cell life span was normal. These data suggest that two distinct genetic mutations perhaps involving enzymes at different steps in the same metabolic pathway may give rise to the same clinical syndrome, "shunt hyperbilirubinemia." As you know, several different types of genetic mutation may give rise to adreno-cortical abnormality states which are clinically similar.

DR. SMITH: I think it has been clearly brought out that although the studies reported have certainly indicated the source of the excessive formation of bilirubin, the basic genetic abnormality is unknown.

†Associate Professor of Medicine.

## DISORDERS OF BILIRUBIN METABOLISM

### RECENT SUMMARIES IN THE LITERATURE

#### *Bilirubin Metabolism:*

1: Lester, R., and Schmid, R.: Bilirubin metabolism, *New Eng. J. Med.*, 270:779, 1964.

2. Stanbury, J. B., Wyngaarden, J. B., and Frederickson, D. S. (eds.): *The Metabolic Basis of Inherited Disease*, Chapter 30, "The Porphyrrias." New York: McGraw-Hill Co., 1960.

#### *Shunt Hyperbilirubinemia:*

1. Israels, L. G. et al.: Hyperbilirubinemia due to an alternate path of bilirubin production, *Amer. J. Med.*, 27:693, 1959.

2. Israels, L. G. et al.: The early appearing bilirubin: Evidence for two components, *J. Clin. Invest.*, 44:42, January 1965.

3. Klaus, D., and Feine, U.: Primary shunt hyperbilirubinemia, *German Med. Monthly*, 10:89, March 1965.

## Sclerosing Cholangitis

DR. PHILIP E. MILLS, JR.\*: The patient, a 74-year-old Caucasian man, came to Moffit Hospital because of jaundice. He had been perfectly well until, four months before admission, he began to notice anorexia and fatigue. A month before admission he noticed jaundice, dark urine and pale stools and began to vomit small amounts of clear fluid. He had lost 25 pounds during the preceding six months and had had pruritus for two or three years. He said that pruritus had disappeared with the onset of jaundice. He had been bothered by a low backache for about a year but had not previously had jaundice, and questioning elicited no other symptoms referable to the gastrointestinal tract. He had had no chills or fever and he knew of no exposure to sources of hepatitis. Cholecystectomy had been carried out when the patient was 45 years of age, because of recurrent pain in the right upper quadrant of the abdomen. He was said to have had cholecystitis and cholelithiasis.

The patient smoked one package of cigarettes a day and usually drank two to four highballs a day. The family history and social history were not contributory. On questioning it was brought out that he had had mild increasing dyspnea on exertion and a slight cough productive of small amounts of sputum for several years. He had had nocturia without dysuria for about the same length of time.

On physical examination the patient appeared

\*Resident in Medicine.



well-developed and well-nourished. He was icteric but in no distress. Vital signs were within normal limits. Scattered rales were heard in the right lung base. The heart was normal to percussion and auscultation. The liver, which was palpable 7 cm below the right costal margin, was firm, smooth and slightly tender. The spleen was of normal size. The nails were slightly brittle and there was loss of the lunulae; there was one spider angioma and the palms were erythematous.

**Laboratory Data:** The hematocrit was 51 per cent and the uncorrected sedimentation rate (Wintrobe) was 38. The urine was brown with a one plus reaction for protein. An occasional hyaline cast was present. The stool was pale yellow and guaiac-negative. Total bilirubin was 20.8 mg per 100 ml with 5.6 mg conjugated. Alkaline phosphatase was 11 SJR† units (normal two to six). Glutamic oxaloacetic transaminase (SGOT) and glutamic pyruvic transaminase (SGPT), prothrombin time, and creatinine and amylase values were within normal limits. Urobilinogen content in a 24-hour specimen of urine was 1 mg. Fasting blood sugar was 110 mg per 100 ml.

At laparotomy the pancreas appeared normal and the liver was firm and green. The common bile ducts extending into the hepatic radicals were thickened and not dilated. The common bile duct was opened, a biopsy specimen was taken, a T-tube was placed and a cholangiogram was performed.

DR. LLOYD H. SMITH, JR.:‡ May we see the x-ray films?

DR. WARREN RUSSELL:§ There are two pertinent x-ray studies. An upper gastrointestinal series demonstrated an apparent widening of the duodenal loop, which is consistent with a mass in the head of the pancreas. This is not diagnostic but is suspicious. The postoperative T-tube cholangiogram is interesting from several standpoints. There is a slight, suggestive irregularity along one wall of the T-tube but it is not very striking. There is a collection of contrast medium in one of the hepatic ducts which appears to be owing either to a very dilated duct or to some extravasation of the contrast medium. From its appearance, I would suspect the latter. The intrahepatic ducts themselves are tapered a little more than we usually see. The common duct is widely patent and the contrast

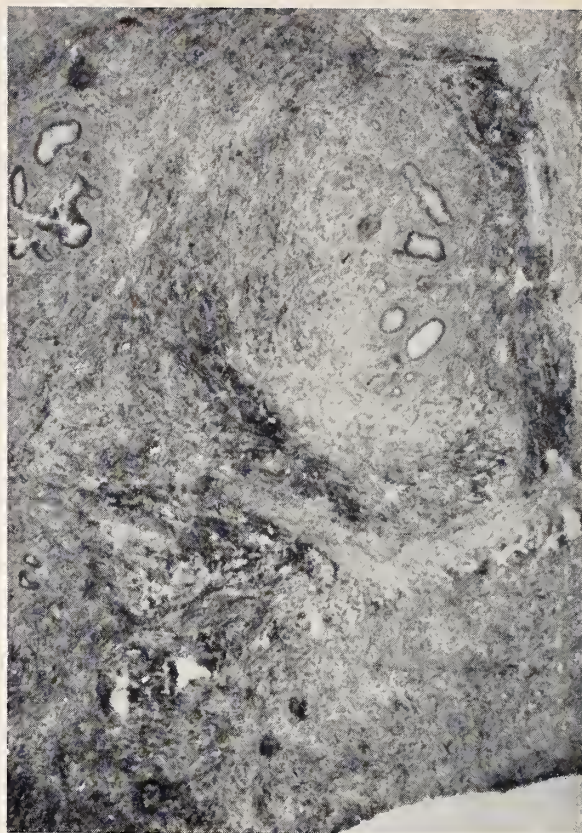


Figure 1.—Frozen section of right hepatic duct. 10x—Hematoxylin and eosin stain.

medium flows into the duodenum without difficulty. DR. OSCAR N. RAMBO:\* This case prompted a series of frozen sections, none of which in our opinion demonstrated tumor. In a small wedge biopsy of the liver, one can see prominent plugs of bile in canaliculae but no evidence of cirrhosis. Scattered throughout the liver were fat-filled hepatic cells, a few nuclear abnormalities, some necrotic cells and bile plugs in addition to pigment in Küpffer cells in the sinusoids. The various biopsies, are represented in Figure 1, which is a photomicrograph of a biopsy from "inside the right hepatic duct." The right hepatic duct showed heavy infiltrates of lymphocytes and in some areas these actually formed follicles. Most of the tissue, however, was fairly dense collagenous scar that was infiltrated by chronic inflammatory cells. A closer view of the ductlike inclusions in this biopsy shows very good differentiation and there are, as you know, in the extrahepatic biliary ducts a number of satellite ducts. The findings, from our point of view, are consistent with those described in sclerosing or stenosing cholangitis. This disease

†Shinowara-Jones-Reinhardt units.

‡Professor of Medicine and Chairman, Department of Medicine.

§Assistant Professor of Radiology.

\*Associate Professor of Radiology.



usually occurs more often in men than in women and there is poor correlation with the presence of gallstones. The origin of this disease is quite obscure. Everything from viruses to the Schwartzman phenomenon has been implicated. I do not know whether there might have been physiologically some stenosis of the segment of duct that contains the T-tube, since this is usually a segmental sclerosis which extends for several centimeters. In summary, this patient had extrahepatic obstruction that had not yet produced biliary cirrhosis, and also inflammation and scarring of several samples of the walls of the common and hepatic bile ducts.

DR. SMITH: Thank you very much. It seemed clear at the beginning that this patient had a surgical problem, but as it turned out it was surgical only in diagnosis. We have called upon Dr. Frank Moody to discuss this problem, particularly the pathogenesis, diagnosis and prognosis.

DR. FRANK G. MOODY:† Primary sclerosing cholangitis seems to be a respectable diagnosis in this patient but it was of interest to me that in his medical work-up this diagnosis was not mentioned, and I suspect this was due to a lack of publicity in the medical literature. But even with a very loose classification there are approximately 35 cases reported in the English literature. My own experience was with two cases at the Cornell University Medical Center. Clinically, this disease presents as progressive jaundice, usually unassociated with pain characteristic of biliary tract disease. However, with close questioning there is usually a complaint of mild discomfort in the epigastrium or in the mid-back, as in the present case. Hepatomegaly is always associated with this condition. The obstructive nature of the icterus is confirmed chemically, with the alkaline phosphatase decidedly elevated and the transaminase normal. Question usually arises as to whether this is obstruction at the level of the cholangioles or in the extrahepatic biliary tree. The differential diagnosis rests among infectious hepatitis in its cholestatic phase, neoplasm, or possibly inflammation, if gallstones are present and the patient has a known history of biliary tract disease or previous biliary tract operation. Because of the insidious onset of jaundice and the frequent presence of a palpable fullness in the epigastrium or a widening of the duodenal loop, exploratory operation often is carried out. At operation the common duct or the common hepatic duct, whichever segment happens to be

involved, is a white, thickened, irregular fibrous cord. It feels very much like a thrombosed varix. On incision into the duct, the wall is extremely thick and fibrotic, the lumen is usually of pinpoint size and there usually is some normal-appearing bile within this lumen. Cultures taken in a few cases have grown *B. coli*.

In the present case there was no bile within the lumen of the duct, but probing into the common hepatic duct did produce a small spurt of normal-appearing bile. In most cases the lumen of the bile duct is smaller than that which we have seen in this particular patient. Biopsy of the specimens of the duct usually show a chronic inflammatory process, and the liver usually is much as Dr. Rambo described it in this particular case.

Postoperatively, in many of the patients, jaundice slowly subsides and they have what appears to be a permanent remission of the disease. Others go on to progressive hepatic failure regardless of treatment.

In a patient whom I followed for a period of four years, the T-tube was left in for a year. Liver function studies never returned to normal but he was not icteric. After removal of the T-tube, he continued to have mildly abnormal results of liver function tests. I encountered a second patient who had had a T-tube in place for four years. It was plugged with calcareous debris and was not functioning. After the tube was removed the patient did quite well.

There is some question as to whether we are dealing with a disease *per se* or a nonspecific reaction of the biliary tree. We know that the bile ducts react this way to injury of any type and occasionally we see this kind of process after operative injury to the duct in removal of the gallbladder. Patients with carcinoma of the bile ducts also have reaction of this type. In fact, one patient who was observed over a period of five and a half years was of this category. He had been operated on three times to maintain a patent biliary tree, the liver biopsy on each occasion demonstrating chronic inflammation. At autopsy a bile duct carcinoma was observed.

It is possible that this disease may represent an auto-immune phenomenon, and some evidence can be mustered to support that possibility. Plasma cells or lymphocytes have been described around the cholangioles within the liver and also within the wall of the extrahepatic ducts, but it is not known whether these are immunologically com-

†Assistant Professor of Surgery.

petent cells. In addition, there is a fairly high association of other diseases that are thought to be related to auto-immunity. In the 25 cases reported since 1954, six of the patients had ulcerative colitis and one had regional ileitis; two had retroperitoneal fibroplasia and another had thyroiditis. Also significant in this regard is that a good response to steroid therapy has been reported in some patients. Two patients whom we have followed did not have steroids and did remarkably well. There are reports in the literature of cases in which patients who did not have T-tube drainage had good relief of symptoms with steroid therapy. One might speculate that the steroids are either interfering with some kind of antigen-antibody process or are nonspecifically suppressing the inflammation associated with this particular disease.

DR. SMITH: We have time for a comment or two on this interesting disease. Dr. Schmid, would you like to make any comment at this time?

DR. RUDI SCHMID:\* I wonder why patients with this disease remain jaundiced after good bile flow has been established through a T-tube?

DR. MOODY: I believe the T-tube may be therapeutic, but I am reluctant to say so because I really

cannot support such a statement. The patients who have had a good response have had T-tube drainage. At operation it is usually necessary to dilate the duct a little to establish drainage.

DR. SMITH: Does the evidence of inflammation in the duct disappear following T-tube drainage?

DR. MOODY: There has not been adequate information on this point.

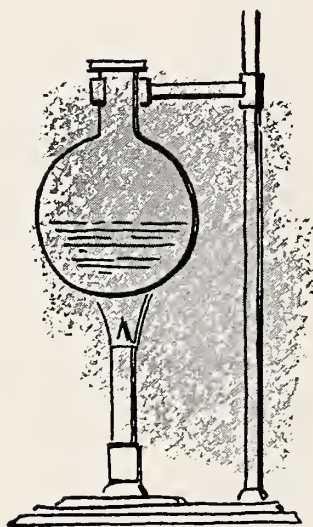
*Editor's follow-up note:* After operation the patient had a wound infection which responded well to antibiotic treatment. He was discharged with prescription of prednisone, 5 mg per day. On the day of discharge the serum bilirubin level was 3.6 mg per 100 ml and alkaline phosphatase was 8 units. Three months later he was feeling much better and at that time the serum bilirubin was 1.0 mg per 100 ml but alkaline phosphatase was 18.4 units. A T-tube cholangiogram done at this time showed persistence of the stricture in the left hepatic duct.

#### SCLEROSING CHOLANGITIS

##### RECENT SUMMARIES IN THE LITERATURE

1. Smith, M. P., and Loe, R. H.: Sclerosing cholangitis, *Amer. J. Surg.*, 110:239-245, 1965.
2. Bartholomew, L. G., Cain, J. C., Woolner, L. B., Utz, D. C., and Ferris, D. O.: Sclerosing cholangitis, *New Eng. J. Med.*, 269:8-12, 1963.
3. Schwartz, S. I., and Dale, W. A.: Primary sclerosing cholangitis, *Arch. Surg.*, 77:439-451, 1958.

\*Professor of Medicine and Chairman, Department of Medicine, University of Chicago.





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For information on preparation of manuscript, see advertising page 2

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## EDITORIAL

### Utilization Review Plan

THE MEDICAL STAFF of almost every hospital in California faces the immediate prospect of participating in the formation of a utilization review plan. Under Public Law 89-97—"Medicare"—the State Department of Public Health will need to "certify" to the Federal Government by about 15 May 1966 that a hospital meets all requirements for "participation"—including a requirement that it have an acceptable plan for review of hospital utilization. Unless it is so "certified," a hospital cannot receive government payment for those services prescribed under the law to almost all persons 65 years of age and over.

The purpose of utilization review in hospitals is primarily educational—to permit the medical staff, by reviewing and analyzing patterns of medical care, to improve its use of the services and facilities of the hospital. If, as a result of utilization review, beds and services come to be used to maximum efficiency, a number of benefits result: More patients can be taken care of, diagnostic services are performed more promptly, delays in scheduling surgical operations are minimized, hospital stays are shortened, convalescent facilities tend to be improved and the total cost of hospitalization is reduced for most patients.

By placing this requirement in the federal law, Congress hoped to improve utilization patterns in all hospitals, thus improving efficiency and holding down costs of hospital care. The law requires an activity which has been recommended by the American Medical Association since 1959, by the

California Medical Association since 1960, and is now a requirement for accreditation by the Joint Commission on Accreditation of Hospitals.

Most medical staffs will have little difficulty in forming a committee to review, "on a sample or other basis," admissions to the hospital, lengths of stays and the use of diagnostic and treatment facilities, for the purpose of achieving the best possible use of the hospital and of other facilities within the community. In some hospitals a medical staff committee will have utilization review as its only function, while in other institutions the utilization review plan may be implemented by existing committees. When a medical staff is too small or the institution does not have an organized staff, a group outside the hospital, which is established by the county medical society, should on request assist the hospital by undertaking to create and administer a utilization review plan.

Every chief of staff and each hospital administrator has received "Guidelines for Utilization Review" developed by the California Medical Association and jointly distributed by the CMA and the California Hospital Association. By following these guidelines, most hospitals may readily establish an acceptable utilization review plan.

In addition to reviewing the general pattern of care, another of the requirements of the law is that the plan must provide for the review of *each* case in which the patient stays in the hospital for "a period of extended duration." The medical staff utilization committee must decide what constitutes such an extended stay. The review of the case must be done no later than one week after the patient has remained in the institution for an "extended duration." If, after consultation with the attending physician, it is found not to be medically necessary for the patient to remain in the institution, then

the attending physician, the hospital and the patient must be notified promptly of this finding. The carrier will cease paying the hospital for service furnished on behalf of the patient beyond the fourth day after the hospital receives notice of such finding.

This legal requirement would appear to be "claims review," rather than an educational activity. Fortunately, the law itself and the implementing regulations are quite flexible. For example, it would be perfectly legal for a medical consultant employed by the carrier to review extended duration cases, referring those which seem questionable to the utilization committee of the hospital or to a committee of the county medical society, for final determination as to "medical necessity." Such an approach would relieve the staff committee of much tedious and time-consuming chart review.

Great flexibility is also permitted and encouraged in other facets of utilization review. For example, medical records committees could do much of the chart review as they now do in many hospitals. Data gathering and sorting operations utilizing electronic processing techniques may be used by utilization committees as a basis for their studies, thus eliminating almost entirely the study of individual records. Eventually, nearly all hospitals will probably use such electronic data processing methods to analyze their patient care and utilization experience.

The activity of a utilization review committee should not be confused with county medical society mediation committee functions. A mediation committee deals with individual cases in which questions are raised or complaints made about charges, coverage and treatment. The mediation committee will continue to handle such cases. A utilization committee recommendation might be considered by a mediation committee in a particular, disputed case. The utilization review committee will primarily concern itself with trends and not with dollars and cents. In the long run, these committees will complement each other.

By studying utilization data, staff committees

could perform an interesting and valuable function—helpful to the medical staff, to the hospital, and most importantly, to the patient, about whose optimal medical care the entire health care team must be vitally concerned.

In performing utilization review studies, the staff committee accepts no greater legal responsibility than do the committees concerned with records, tissues or credentials. Under California law, such committees, acting in good faith, and "without malice, prejudice or caprice," are legally exempt from civil liability. Regardless of the fact that it is required by law, utilization review should be a responsibility of each medical staff, and it should be carried out in a manner which reflects the continuing concern of physicians for the public health and welfare.

## A New Feature

ELSEWHERE IN THIS ISSUE [page 124] we publish discussions of two cases selected from the weekly Medical Staff Conferences held at the University of California Medical Center, San Francisco. We plan to present interesting cases from these conferences in succeeding issues.

For some time, *California Medicine* has been looking for a regular monthly supply of well turned out clinical conferences to meet a recommendation by the Committee on *California Medicine* that material of this kind be added to the continuing medical education function of your journal.

Under the general supervision of Dr. Lloyd H. Smith, Jr., Professor of Medicine and chairman of the Department of Medicine, the reports are being prepared from transcripts by two assistant professors in the department, Dr. Martin J. Cline and Dr. Hibbard E. Williams.

We are pleased to offer this new feature and we welcome readers' comments.



# California Medical Association



## NOTICES AND REPORTS

### Council Meeting Minutes

*Tentative Draft: Minutes of the 516th Meeting of the Council, Hilton Inn, San Francisco, 11 December 1965.*

The meeting was called to order by Chairman Anderson in the Hilton Inn, San Francisco, Saturday, 11 December 1965, at 9:45 a.m.

#### Roll Call

Present were President Teall, President-Elect MacLaggan, Speaker Quinn, Vice-Speaker Telford, Secretary Hosmer and Councilors Isenhour, Wilson, Melone, Todd, Gooel, Bullock, O'Connor, Rogers, Maguire, Burnett, Richard S. Wilbur, Miller, Watts, Fenlon, Kay, Kaiser, Anderson, Yant, Grunigen and Shaw. Absent for cause were Editor Dwight L. Wilbur, and Councilors Taw, Ham and Doyle.

A quorum present and acting.

Present by invitation were Messrs. Clancy, Collins, Klutch, Eberlein, Thomas, Goldman, Whelan, Blackley, Bowman, Clark, Doctor Miller, Miss Price, Mrs. Redfern and Mrs. Griffith of CMA staff; Messrs. Hassard and Huber, legal counsel; component society executives Scheuber of Alameda-Contra Costa, Rideout of Butte-Glenn, Geisert of Kern, Lingerfelt of Fresno, Baker of Los Angeles, Collins of Marin, Bannister of Orange,

Dochterman of Sacramento, Nute of San Diego, Neick of San Francisco, Marvin of Santa Barbara, Wood of San Mateo, Donovan of Santa Clara, Thompson of San Joaquin, Brown of Sonoma, Walters of Riverside, Donmyer of San Bernardino, Colvin of Monterey, Funk of Solano; Doctor Lester Breslow, director of the State Department of Public Health; Mr. Warren Thompson, director, and Doctor Richard Young, medical director, of the State Department of Rehabilitation; Doctor Robert Radl of the State Department of Employment; Mrs. Jeanette Gentile, president of the California Medical Assistants Association; Doctor William Thompson and Messrs. Nyren, Wahlberg, Pottloff, Heller and Babb of California Physicians' Service; Messrs. Read, Putnam and Brown of the Public Health League; Mr. Jerry Gould, AMA field representative; Mr. Joseph Zem, treasurer of the California Hospital Association; Doctors Warren Bostick, T. Eric Reynolds, William Larsen, Donald Harrington, Donald Hause, Burt Davis, Nicholas Oddo, Bert Halter, George Herzog and others.

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RALPH C. TEALL, M.D. . . . .	President
JAMES C. MACLAGGAN, M.D. . . . .	President-Elect
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MATTHEW N. HOSMER, M.D. . . . .	Secretary
DWIGHT L. WILBUR, M.D. . . . .	Editor
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### 1. *Recognition of John Hunton*

The members of the Council and guests stood for a moment of silence in memory of John Hunton. Mr. Hunton, who had only recently completed 25 years of service to the California Medical Association, died suddenly of a heart attack on 2 December 1965. Those present expressed their sorrow at the loss of Mr. Hunton.

**ACTION:** *Voted to authorize a suitable gift to be presented to Mrs. Pia M. Hunton.*

### 2. *Minutes for Approval*

On motion duly made and seconded, minutes of the 515th meeting of the Council, held 30 and 31 October 1965, were approved with the following corrections: Councilor Miller should be listed as present; strike out "by Assemblyman Casey" on second line, paragraph 3, page 3.

### 3. *Membership*

(a) A report of membership as of 8 December 1965 was presented and ordered filed.

(b) On motion duly made and seconded, three applicants were voted election to Associate Membership. These were: Vera B. Fryling, Alameda-Contra Costa County; William S. Lawler, Riverside County; Jerrold K. Longerbeam, Riverside County.

(c) On motion duly made and seconded, three members were voted election to Retired Membership. These were: Luther Russell Hansen, Alameda-Contra Costa County; Francis M. Smith, San Diego County; Edward B. Radford, Alameda-Contra Costa County.

(d) On motion duly made and seconded, a reduction of dues was voted for six members for reasons of prolonged illness or postgraduate education.

### 4. *Authorization for Signature Changes on Bank Accounts*

Mr. Hassard informed the Council of the difficulty in processing checks due to the death of Mr. John Hunton. Permission was asked to add two staff names with titles to the signature cards of banks in which CMA monies are deposited.

**ACTION:** *Voted to authorize the addition of the names of Robert L. Thomas and William M. Whelan to the CMA "bank signature cards" and that both of these executive staff members be given the title of "Assistant Secretary"—all other authorized signers to remain as such.*

### 5. *Report of the President*

President Teall reported on several meetings he had attended or addressed since the last meeting of the Council. These included visits to county and district societies, the White House Conference on Health, conference with welfare and health fund administrators in southern California, California College of Medicine, and others.

Doctor Teall also informed the Council that he had been recommended by the AMA, and subsequently appointed, to an ad hoc advisory committee to the United States Commissioner of Welfare (Dr. Ellen Winston). Purpose of the committee is to advise the Commissioner on the regulations to be drawn for Title XIX of Public Law 89-97. (California has already passed enabling legislation to implement Title XIX through Assembly Bill 5.)

### 6. *Committee for Emergency Action*

President Teall reported that the Committee for Emergency Action had three meetings (two of them by phone conference) since the last Council session. Rapidly changing developments with regard to Public Law 89-97 and other legislative problems necessitated immediate action.

The CMA was asked to submit names of two physicians to serve on the new Health Review and Program Council established under the provisions of Assembly Bill 5. President Teall reported that the Committee for Emergency Action recommended the names of Doctor Albert G. Miller of San Mateo and Robert Watson of Los Angeles.

The committee also approved a tentative statement on utilization review plans for the guidance of California Physicians. Doctor Teall emphasized that this was a brief interim statement and that guidelines for utilization review plans were being developed by the CMA Task Force on Public Law 89-97.

Third meeting of the Committee for Emergency Action was held in Philadelphia with physicians from the Los Angeles area. Purpose of the meeting was to discuss a series of resolutions which had been submitted to the AMA House of Delegates. President Teall reported that several of the resolutions were modified and that the California delegation subsequently supported them.

**ACTION:** *Voted to affirm the actions taken by the Committee for Emergency Action.*

### 7. *Utilization and Review Plans*

Tentative draft of proposed CMA guidelines for



utilization review plans for hospital staff and extended care facilities was presented to the Council. Members discussed thoroughly the development of the utilization function through the CMA Guiding Principles for Physician-Hospital Relationships and other activities. Doctors Teall and Anderson and others presented the statutory requirements for utilization review plans under Public Law 89-97 and Assembly Bill 5. After suggesting numerous changes in the tentative draft and recognizing need for further editing, the Council passed the following motion.

**ACTION:** *To give authority to the Council Task Force on Public Law 89-97 and its Executive Committee to proceed with the development of guidelines and background educational material for physicians' use in developing utilization review plans to include a prototype utilization review plan; to consult with appropriate groups in the development of materials; and to distribute the document and its accompanying materials.*

#### 8. Federal Legislation on Laboratory Animals

President Teall reported on a recommendation of the Scientific Board that the CMA express opposition to proposed federal legislation which would seriously hamper progress in medical research by restricting the use of laboratory animals. Draft of a proposed letter on the subject addressed to Representative Oren Harris, chairman of the House Committee on Interstate and Foreign Commerce, was read by Councilor Bullock. The suggestion was made that the letter, copies of which are to be sent to members of the committee and others, should be checked with the AMA Washington office.

**ACTION:** *Voted approval of the letter and its widespread distribution after appropriate editing.*

#### 9. Department of Public Health

Doctor Lester Breslow, newly-appointed Director of the State Department of Public Health, expressed appreciation for the medical leadership provided by CMA in recent months and for the intention of CMA to provide some meaningful guidelines for utilization review plans. The department's role in the implementation of Assembly Bill 5 was reviewed by Doctor Breslow. He noted that some persons in state government were revising their previous attitudes toward physicians' charges and other health care costs, by recognizing that adequate reimbursement was an important criterion with respect to the provision of medical care.

Mr. Warren Thompson, director, presented a

progress report on the development of this two-year-old state department. He emphasized that although many of the rehabilitation functions were already being provided in other departments of government, the establishment of a centralized Department of Rehabilitation has allowed better coordination and improved services.

#### 11. State Board of Medical Examiners

Doctor Nicholas Oddo, board president, informed the Council that Senate Bill 1203, scheduled for interim hearing, may be postponed or not heard. The questionnaire sent to all hospitals in California—as a step in implementing Senate Bill 405—has generated a good response thus far. As of 9 December, 400 replies had been received. Doctor Oddo emphasized again that the Board will exercise caution in implementing Senate Bills 400 and 403. Nominees for the district review committees, established under 1965 laws, have been considered and appointments will be made soon.

#### 12. California Hospital Association

Mr. Joseph Zem, CHA treasurer, reported that the California Hospital Association is scheduling a series of medicare and Casey Bill "orientation seminars" for its membership throughout the state. Three meetings will be held: 16 February in Los Angeles, 17 February in Fresno, 18 February in San Francisco. Various aspects of Public Law 89-97 and Assembly Bill 5 will be presented during this special series.

#### 13. California Physicians' Service

Doctor William Thompson, board chairman, noted that CPS is now working on "medigap" programs to offer as a supplement to over-65 coverage under Public Law 89-97. He also reported that efforts are still being made to upgrade fee schedules in keeping with direction of the House of Delegates, and that by the end of this year at least 75 per cent of all commercial contracts will be on the "D" schedule or better.

Doctor Thompson reaffirmed that if CPS is selected as a "fiscal intermediary" under either Title XVIII or Title XIX of P.L. 89-97, it is willing to administer the programs on a "usual and customary" fee basis, utilizing county medical society review and mediation bodies in arriving at proper determinations in this regard. Discussion was held on the role of county society mediation committees

with respect to charges for, and utilization of, professional services, particularly under Part B, Title XVIII, P.L. 89-97.

**ACTION:** *Voted to authorize Doctor Thompson and Council representatives on the CPS Board of Trustees, in cooperation with selected chairmen of county society mediation committees, to prepare guide-lines on the role of mediation and other committees of the county society under Public Law 89-97, such guidelines to be presented to the Council for action.*

#### 14. Medical Executives Conference

Mrs. Olive Neick introduced Mr. Ed Collins, new executive secretary of the Marin Medical Society. She announced that the Communications Committee of the Conference had voted to offer its services to Mr. Hassard and to the CMA communications staff in preparing an information program for the profession and the public on Titles XVIII and XIX of P.L. 89-97.

#### 15. California Delegation to the AMA

Doctor Burt Davis, newly elected chairman of the California AMA delegation, reported on the recent clinical session in Philadelphia. He paid tribute to John Hunton's staff activities in support of the delegation for many years.

The importance of having regular meetings of the CMA Council and the AMA delegation prior to national AMA conventions was stressed by Doctor Davis.

#### 16. Ad Hoc Committee to Study Quality of Radiologic Films

The assignment given to this committee by the Council has been completed, according to the chairman, Doctor Burt Davis. Excellent cooperation was secured from the California Society of Internal Medicine, the California Academy of General Practice, the Western Orthopedic Association and the California Radiological Society in designating members of the four review teams. Criteria for evaluation of films were established and all films for which charges had been made to CPS for a three-month period were requested. Ninety-eight per cent of the films were received.

Doctor Davis noted the following conclusions of the committee: (1) There is no indication that physicians are making charges for films not made or for services not performed, (2) The findings suggest that there is not a sufficient difference in the adequacy between the films submitted by physicians in the various specialties to warrant any difference in fee payments. CPS Trustees should

be requested (a) to continue the practice of paying uniform fees for radiologic services, and (b) that the medical director of CPS be authorized to make occasional spot checks of films for which claims were submitted, (3) As in all such studies, certain problem areas were uncovered which should be handled through consultation with the Scientific Board and the specialty groups involved, in order to encourage educational programs.

**ACTION:** *Voted to approve the report of the committee.*

#### 17. Report of the President-Elect

Doctor James MacLaggan reported on his recent public speeches and visits to component societies in northern California.

#### 18. Status Reports on 1965 Resolutions

Chairman Anderson reminded members of the Council that a status report on 1965 resolutions must be submitted to members of the House of Delegates in the near future.

**ACTION:** *Voted to authorize staff to bring up to date actions on 1965 resolutions and distribute this report to delegates and alternates.*

#### 19. Finance Committee

Doctor Harold Kay presented a written report on progress in formulating a budget for 1966-67 fiscal year. The committee is continuing its thorough review of the proposed budget and will submit to the Council (at its January meeting) a budget for final action and submission to the House of Delegates.

Various elements within the budget were discussed at length, such as the CMA contribution to AMA-ERF.

**ACTION:** *Voted to defer until the January meeting of the Council any definitive action regarding contributions to AMA-ERF.*

The committee reported that for some years, the Constitution of the Association has specified that \$1.00 of the dues of each active member be set aside for the Physicians Benevolence Fund. Inasmuch as the assets of the Fund appear to be sufficient to make it self-sustaining, the committee recommended deletion of the item.

**ACTION:** *Voted to recommend to the House of Delegates that the \$1.00 per active member for the Physicians Benevolence Fund be eliminated.*

CMA financial participation in the Tumor Tissue Registry (housed in Los Angeles County Hospital) was described. Action was taken several



years ago to phase out the CMA participation in stages of \$2,000 per year.

**ACTION:** *Voted to continue the phasing out process on financial participation of the CMA toward the Tumor Tissue Registry.*

Doctor Kay also noted a letter addressed to him by Doctor Bert Halter, chairman of the Medical Staff Survey Committee, asking consideration for some financial compensation to members of his committee who survey medical staffs. Doctor Kay expressed his view that the request required a policy definition by the Council before the Finance Committee could consider the financial aspects.

**ACTION:** *Voted to defer action on the request pending consultation with the officers of the California Hospital Association.*

#### 20. *Liaison Committee to CPS*

The committee met on 9 November to consider the request of the Council that it review and make recommendations on the prevailing fee concept being developed by Blue Shield. The liaison committee recommended that a pilot study be undertaken in several areas of the state which desire to participate in such a study. The pilot study will be conducted jointly by the CMA Bureau of Research & Planning and the CMA Committee on Fees. Technical assistance will be provided by CPS.

**ACTION:** *Voted to approve the report of the committee and to authorize the pilot study as outlined.*

#### 21. *Request from the Humboldt-Del Norte County Medical Society*

In a letter to CMA from Doctor Robert L. Devine, the Humboldt-Del Norte County Medical Society requests financial support to assist the North Coast Health Facilities Planning Association.

**ACTION:** *By consensus the letter was referred to the Commission on Hospital Affairs.*

#### 22. *Committee on Committees*

Doctor MacLaggan discussed CMA participation in a data processing study in cooperation with the Hospital Planning Association of Southern California, the California Hospital Association, and others. A three-man CMA committee was recommended to work with the other agencies. Names submitted were Doctors James C. MacLaggan, chairman, Glenn Pope and Joseph Telford.

**ACTION:** *Voted to approve the recommendation of the Committee on Committees.*

#### 23. *Commission on Public Agencies*

A statement on "Medical Supervision of Organic Phosphate Pesticide Workers"—prepared by the Committee on Occupational Health and Rehabilitation—was presented to the Council for approval.

**ACTION:** *Voted to approve the statement subject to approval of the Committee on Scientific Information.*

Staff was directed to write to the Santa Cruz Medical Society and the Alameda-Contra Costa Medical Association expressing the appreciation of the Council for the initial work of these two societies in formulating the above statement.

#### 24. *Commission on Community Health Services*

Doctor Kay presented a request of the Committee on School Health that the President of the CMA suggest to the Governor of California that a member of the CMA Committee on School Health be named to the advisory committee established under the provisions of A.B. 1331.

**ACTION:** *Request approved.*

#### 25. *Commission on Communications*

Doctor Todd reported on several items of business discussed by the Commission on 10 December. He noted the communications activities of CMA, particularly regarding Assembly Bill 5 and Public Law 89-97.

The Commission recommended that a special communications effort be made to keep California delegates and alternates to AMA informed of current CMA activity.

**ACTION:** *Voted to approve recommendation of the Commission.*

The questions surrounding CMA participation in the California Interagency Council on Cigarette Smoking and Health have now been resolved, so the Commission plans to proceed with its \$3,000 financial commitment. However, the Commission recommended to the CMA Council that future involvement of the California Medical Association in the Interagency Council on Cigarette Smoking and Health be transferred from the Commission on Communications to the Commission on Community Health Services.

**ACTION:** *Voted to approve the transfer to the Commission on Community Health Services.*

#### 26. *Scientific Board*

Doctor Edward Shaw reported on the full-day session of the Board held on 4 December.

A statement on coronary care units was submitted for approval of the Council. Suggestions were made that if this statement were approved that a complementary statement already prepared by the Committee on Other Professions—be published with it.

**ACTION:** *Voted to approve the statement.*

The Scientific Board recommended that a new monthly bulletin entitled "What Goes On," be published and mailed to all doctors in California. This would be supported by two pages of advertising from Lederle Laboratories at no cost to CMA. This new bulletin would list available courses and other continuing education opportunities with geographical and subject area breakdown.

**ACTION:** *Voted to grant approval to the project.*

With regard to financial support of continuing medical education in California, the Scientific Board recommended that in the future, when present commitments are over, contributions to CMA from Audio-Digest be distributed equally to the departments of continuing medical education in all California medical schools.

**ACTION:** *Voted to approve the intent of the recommendation and to refer it to the California Medical Education & Research Foundation for its information.*

The Board also recommended that the \$10 per member sum which in the past has been given to AMA-ERF for general medical school support be given in the future to departments of continuing medical education of all California Medical Schools. (House of Delegates action would be required.)

**ACTION:** *Voted to defer action on this recommendation until the January meeting of the Council.*

## 27. Resolutions from Los Angeles County Medical Association

Correspondence from Doctor Harold Wilkins,

LACMA secretary-treasurer, was presented to the Council. CMA action was requested on two resolutions passed recently by the LACMA Council.

The first resolution asked that the CMA accept as policy the report of the Reference Committee on Legislation and Public Relations, AMA House of Delegates, 3 October 1965.

**ACTION:** *Voted that the request be tabled.*

The second resolution requested that the CMA not take a policy position on the CAL-MED program until sufficient information and time is given to component societies for detailed study.

**ACTION:** *Voted to inform LACMA, in essence, no CMA policy position has yet been approved on the CAL-MED concept and that it is hoped component societies will study the proposed program in detail.*

## 28. CMA Representatives on the California Committee on Fitness

President Teall presented a request from the State Department of Education asking for three representatives to attend the annual meeting of the California Committee on Fitness in San Mateo, 13 and 14 May. Chairman Anderson directed that the request be referred to the Committee on Committes.

## 29. Report of Legal Counsel

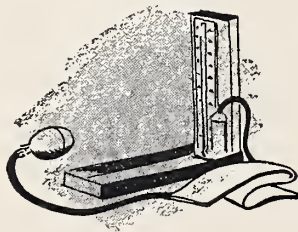
Mr. Hassard reported on the current status of three lawsuits involving the California Medical Association.

## Adjournment

There being no further business to come before it, the meeting was adjourned at 4:25 p.m. in memory of Mr. John Hunton.

CARL E. ANDERSON, M.D., *Chairman*

MATHEW N. HOSMER, M.D., *Secretary*





## Medical Radio Conferences

SEYMOUR M. FARBER, M.D.

*Dean of Educational Services and Director of Continuing Education, Health Sciences, University of California School of Medicine, San Francisco.*

RESEARCH IN RECENT YEARS has been so productive that physicians have to exert great effort to keep up with new practices and procedures. To get word of the latest developments in the medical field to physicians in outlying districts as well as to those in larger communities unable to take the time to attend formal courses, the Division of Continuing Education in Medicine and the Health Sciences at the University of California Medical Center, San Francisco, initiated a series of two-way radio broadcasts in the fall of 1963. These broadcasts can disseminate information to a large audience in a limited amount of time. To some extent they can take the place and save the time of traveling to large communities to attend postgraduate courses. With them the physician is relieved of much of the burden of reviewing hundreds of articles—there were some 130,000 listed in the 1963 *Index Medicus*—to find those relevant to his daily practice.

It has been our experience that the medical radio conferences have been successful in bringing together medical school faculty and practicing physicians within a 500-mile radius in free and open discussions about such current medical problems as breast cancer, emphysema and the treatment of ulcers.

The most important element in the success of programs in this medium is the question-and-answer sessions which are an integral part of each

broadcast. These sessions permit a participating physician to ask a question and receive an answer in much the same way he would if he were in actual attendance at a program at the Medical Center.

Although it is necessary to be present at a participating hospital to take part in the question-and-answer portion of the program, any physician within broadcast range can listen in his car, home or office. Many hospitals also tape each program so that physicians may hear any broadcast at their convenience.

Currently, more than 800 physicians are participating in the series and more than 1,500 copies of speakers' lecture notes and case presentations are mailed each week to participating hospitals. To date, the greatest response has been from physicians in general practice, although large numbers of internists, surgeons, urologists, radiologists and house staff personnel are also participating.

The medical radio conferences are but an indication of the use which must be made of new audio-visual media if new knowledge is to be disseminated regularly to the quarter-million physicians in this country. Television, both open and closed circuit, is being used as a teaching device at many educational institutions. It has been effectively utilized, for example, at the University of Utah School of Medicine for postgraduate education. Both audio and visual tapes can be produced at medical centers on a variety of subjects and made available in local communities to be played back when a physician is able to take a few minutes out of a busy schedule.

Many physicians in California, however, have indicated they prefer to participate in two-way broadcasts; and in a state such as ours, with wide geographical variations and with communities hundreds of miles from the nearest medical center, the medical radio conferences have been a major step forward in bringing the most recent concepts into outlying districts with a minimum of expenditure.

## In Memoriam

ABBOTT, LEROY C., San Francisco. Died 19 December 1965, in Coronado, aged 75. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1914. Licensed in California in 1914. Doctor Abbott was a retired member of the San Francisco Medical Society and the California Medical Association, and an associate member of the American Medical Association.



BRIGGS, WILFORD M., Monrovia. Died 14 December 1965, in Duarte, aged 70, of heart disease. Graduate of the University of Oregon Medical School, Portland, 1924. Licensed in California in 1925. Doctor Briggs was a member of the Los Angeles County Medical Association.



GALLIGAN, CHARLES A. JR., Carmel Valley. Died 21 December 1965, aged 65. Graduate of Tufts College Medical School, Boston, Massachusetts, 1926. Licensed in California in 1931. Doctor Galligan was a retired member of the Monterey County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



GARTH, WILLIAM LEROY, La Jolla. Died 10 December 1965, in La Jolla, aged 72. Graduate of Stanford University School of Medicine, Palo Alto-San Francisco, 1925. Licensed in California in 1925. Doctor Garth was a retired member of the San Diego County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



HIDY, KLORE WILLIAM, Alamo. Died 14 August 1965, aged 75, of arteriosclerosis and diabetes mellitus. Graduate of Indiana University School of Medicine, Indianapolis, 1911. Licensed in California in 1914. Doctor Hidy was a retired member of the San Joaquin County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



JELLEN, JOSEPH, Los Angeles. Died 11 December 1965, in Los Angeles, aged 57, of heart disease. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1933. Licensed in California in 1936. Doctor Jellen was a member of the Los Angeles County Medical Association.



KELETY, EUGENE, Bell Gardens. Died 20 December 1965, in Pico Rivera, aged 55, of heart disease. Graduate of Deutsche Universitat Medizinische Fakultät, Prague,

Czechoslovakia, 1935. Licensed in California in 1952. Doctor Kelety was a member of the Los Angeles County Medical Association.



KIRCHNER, ARTHUR ADOLPH, Los Angeles. Died 3 January 1966, in Los Angeles, aged 62, of cerebral vascular accident. Graduate of Northwestern University Medical School, Chicago, Illinois, 1929. Licensed in California in 1929. Doctor Kirchner was a member of the Los Angeles County Medical Association.



MCGUIRE, JAMES BALFOUR, Mt. Shasta. Died 3 September 1965, in Redding, aged 74, of coronary thrombosis. Graduate of the University of Manitoba Faculty of Medicine, Winnipeg, Canada, 1921. Licensed in California in 1926. Doctor McGuire was a member of the Siskiyou County Medical Society.



PLAYER, LIONEL PAGET, Pacific Grove. Died 16 December 1965, in San Francisco, aged 85. Graduate of Tulane University School of Medicine, New Orleans, Louisiana, 1914. Licensed in California in 1915. Doctor Player was a retired member of the San Francisco Medical Society and the California Medical Association, and an associate member of the American Medical Association.



SCHMAHL, PHILLIPP J. R., Redlands. Died 23 December 1965, in Redlands, aged 80. Graduate of New York Medical College, Flower and 5th Avenue Hospitals, New York, 1911. Licensed in California in 1948. Doctor Schmahl was a retired member of the San Bernardino County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



TAMBURELLO, NINO E., Santa Barbara. Died 21 December 1965, in Santa Barbara, aged 65. Graduate of Facoltà di Medicina e Chirurgia dell'Università di Roma, Roma, Italy, 1923. Licensed in California in 1947. Doctor Tamburello was a retired member of the Santa Barbara County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



YEIN, CHUNG SANG (CHARLES), Carmichael. Died 18 December 1965, in Sacramento, aged 41, of primary hepatoma. Graduate of West China Union University School of Medicine, Chungtu, Szechwan, China, 1946. Licensed in California in 1963. Doctor Yein was a member of the Sacramento County Medical Society.



*See complete program in this issue following page 160*



# ANNUAL SCIENTIFIC ASSEMBLY

**MARCH 19-23, 1966\***

**LOS ANGELES**

*current concepts in therapy*

**POINT AND COUNTERPOINT**

*featuring—*

**RENAL FAILURE**

**CORONARY ARTERY DISEASE**

**GASTROINTESTINAL HEMORRHAGE**

- *among the distinguished speakers  
presenting their "current concepts in therapy":*

- CHARLES K. FRIEDBERG, M.D., Columbia University
- BERNARD LOWN, M.D., Harvard University
- BELDING H. SCRIBNER, M.D., University of Washington
- OWEN H. WANGENSTEEN, M.D., University of Minnesota

A VARIETY OF EVENTS in addition to those directly related to this year's theme WILL HIGHLIGHT YOUR 1966 ANNUAL SCIENTIFIC ASSEMBLY . . . eighteen medical specialty section meetings . . . seven special conferences . . . motion picture symposia . . . color TV programs . . . scientific and technical exhibits.

\*House of Delegates and Special Conferences start Saturday, March 19.

# *16th annual regional postgraduate institute*

*OJAI VALLEY INN  
Ojai  
March 11-12, 1966*

## **WEST COAST COUNTIES**

Presented cooperatively by West Coast Counties Medical Societies, Continuing Education in Medicine and the Health Sciences, University of California San Francisco Medical Center, and the Committee on Continuing Medical Education, California Medical Association.

**HOST:** Santa Barbara County Medical Society.

**Regional Chairman:** George J. Wittenstein, M.D.,  
222 West Pueblo Street, Santa Barbara.

**INSTITUTE FEE:** \$15.00. For additional information contact Continuing Medical Education office, California Medical Association, 693 Sutter Street, San Francisco 94102. All California Medical Association members and their families are cordially invited to attend.

**GUEST SPEAKER:** Claude Welch, M.D., Clinical Professor of Surgery, Harvard Medical School; Visiting Surgeon, Massachusetts General Hospital.

## **INDICATIONS FOR SURGICAL INTERVENTION— THE DIFFICULT DECISION**

**FRIDAY, MARCH 11**

### *Morning Session*

#### **HIATUS HERNIAS**

I refer to the surgeon when—Howard Shapiro, M.D.

I feel I should operate when—Orville F. Grimes, M.D.

#### **PEPTIC ULCER**

The patient needs surgical treatment if—Hugo C. Moeller, M.D.

I would agree to operate if—Claude Welch, M.D.

#### **GALLBLADDER DISEASE**

Surgical help is necessary because—Howard Shapiro, M.D.

I would agree to surgery because—Robert Combs, M.D.

### *Afternoon Session*

#### **COLITIS, DIVERTICULAR DISEASE AND OTHER PROBLEMS IN THE COLON**

I think we have reached the point for surgery since—John Carbone, M.D.

I would agree to a surgical approach since—Walter Birnbaum, M.D.

**CONCURRENT WORKSHOPS** (you may go to one of your choice):

Case discussions: West Coast Counties participants with the faculty.

A. **Biliary System**—John Carbone, M.D., Claude Welch, M.D.

B. **Colon and Rectum**—Walter Birnbaum, M.D., Howard Shapiro, M.D.

C. **Esophagus and Stomach**—Orville F. Grimes, M.D., Hugo C. Moeller, M.D.

**SATURDAY, MARCH 12**

### *Morning Session*

#### **THE INFECTED URINARY TRACT**

Surgical assistance is necessary when—Allan M. Unger, M.D.

I agree to a surgical approach when—Donald R. Smith, M.D.

#### **NONMALIGNANT PULMONARY PROBLEMS**

I feel the surgeon can help if—Roger H. L. Wilson, M.D.

I would be willing to use a surgical approach if—Orville F. Grimes, M.D.

#### **THYROID NODULES**

Certain of these should be explored because—Francis Greenspan, M.D.

I would surgically explore these patients because—Claude Welch, M.D.

### *Afternoon Session*

#### **THE POOR RISK PATIENT**

**Cardiac, pulmonary and metabolic problems**—Walter Birnbaum, M.D., John Carbone, M.D., Robert Combs, M.D., Francis Greenspan, M.D., Hugo C. Moeller, M.D., Donald R. Smith, M.D., Allan M. Unger, M.D., Claude Welch, M.D., Roger H. L. Wilson, M.D.

**CONCURRENT WORKSHOPS** (you may go to one of your choice):

Case discussions: West Coast Counties participants with the faculty.

A. **Lungs**—Orville F. Grimes, M.D., Roger H. L. Wilson, M.D.

B. **Thyroid**—Robert Combs, M.D., Francis Greenspan, M.D.

C. **Urinary Tract**—Donald R. Smith, M.D., Allan M. Unger, M.D.



# WOMAN'S AUXILIARY

to the California Medical Association



## International Health Activities

THE MEMBERS of the Woman's Auxiliary to the California Medical Association have accepted as their particular service to Direct Relief Foundation the collection of sample drugs, bandages, hospital gowns and linens, baby foods and food supplements as well as surgical and dental instruments and supplies. These items are sent or taken to the Foundation's Santa Barbara warehouse where a staff of volunteers under the direction of a licensed pharmacist sorts and packs them. Shipments are then made in response to specific requests by physicians in needy areas.

About 50 per cent of the drugs used in this project are donated by manufacturers, the remainder by the medical auxiliaries. Interest in collecting these vital supplies has been intensified this year by the realization that enormous shipments are being made to South Vietnam through a cooperative effort with Project Handclasp. In 1965 medicines valued at over three million dollars were sent to this one troubled area alone. This volunteer activity is carried on in their free time by Navy physicians, who have expressed deep appreciation of the aid given. Army and Marine medical personnel have also written to thank Direct Relief Foundation for helping in this way to win the good will of the civilian population.

Since each county Auxiliary has its own method for collecting and sending drugs to Santa Barbara, physicians interesting in joining the program begin by getting in touch with the International Health Activities chairman of their local organization.

Physicians' help is also needed for another special project for which Auxiliary members have accepted responsibility. Used text books are provided for HOPE, the peacetime hospital ship which carries medical teaching-healing teams to underdeveloped areas. Physicians themselves must

determine the value of the books in this day of rapid obsolescence. Anyone who can supply texts of current value should notify officers of the local Auxiliary. Project HOPE is now serving three continents, where it has trained 3,000 physicians, treated over 100,000 persons, conducted some 6,000 major operations, and vaccinated over a million people, according to the last published report.

Aid is also given by medical auxiliaries to the World Medical Association in its doctor-to-doctor journal program. Once again Auxiliary members can provide information about this, even if the local county medical society is not participating in this particular effort.

Finally the CMA Woman's Auxiliary gives assistance to the Catholic Medical Missions Board. All county International Health Activities chairmen receive instructions for rolling bandages, folding compresses and making hospital gowns which are sent to all the areas of the world served by this AMA-recommended agency.

Apart from the above programs, some local auxiliaries have themselves taken more particular and direct interest in some areas of the world and have made shipments of supplies to Mexico, Chile, Nicaragua, Ecuador, Haiti, Hong Kong and Vietnam. Often these particular interests are sparked by some local physician who has donated time to an overseas aid team or has served as a medical missionary.

The effort to implement the wish of the American Medical Association that every physician who comes to the United States to visit or study be a guest in an American physician's home has had happy results. When possible, physicians and their wives from abroad are invited to attend Auxiliary meetings as speakers and guests.

MRS. JAMES W. MOORE

*International Health Activities Chairman*

# INFORMATION

## Professional Problems in Federalized Health Care Abroad

*A Report of the Bureau of Research and Planning, California Medical Association*

### Introduction

Recent passage of Medicare legislation by Congress presents the American people with an entirely new approach to financing and provision of medical care. This significant step, while taken long after most other Western countries and many of the developing countries, is an indication of the ever-increasing responsibility assumed by the government in the financing of health care, regardless of need. Observation of many already established nationalized programs gives the United States the advantage of being able to learn from others' experiences and avoid their mistakes. Difficulties and discontent with organizational details of any program, its financial arrangements, distribution of authority and qualitative controls, still characterize most Federal programs.

The following discussion deals with some of the more frequent problems which aggravate federalized legislative enactments—problems which have thus far been met with lengthy political debate, periodic negotiation and occasional mass protest by physicians. No attempt is made to describe the various systems beyond their relevance to the particular problems they generate.

The specific problems to be considered in this discussion, listed in approximately the order of their occurrence within various socialized programs, are as follows: 1) Inadequate Physician Remuneration; 2) Decline of Professional Status and Subsequent Authority of Physicians; 3) Dominance of Political Decisions in Allotting Funds; 4) Bureaucracy of Federal Control; and 5) The Patients' Perspective: Impersonality of Care.

### 1. Inadequate Physician Remuneration

The problem of inadequate physician income has undoubtedly contributed more to the psychological weakening of the program than has any other problem. Physicians in many countries have in the past united in angry protest against their respective governments. The volume and nature of their demonstrations, referring to such cases as the mass strikes occurring in Belgium, Italy, France and Mexico, have won considerable sympathy among American physicians. The intensity of strife possibly induced

further objections to facets of the program among the physicians, if not complete disenchantment with it.

### GREAT BRITAIN

Recently, British physicians have had much to say on this subject. Dissatisfaction with salary increases issued this Spring by the government motivated Britain's GP's (numbering 24,000 out of 64,000 physicians in the National Health Service and 600 physicians who maintain a totally private practice), to become involved in the most serious crisis that has threatened the National Health Service since its inception in 1948. The GP's presented a united front and, on threat of resigning from NHS, demanded that the government pay them a minimum weekly average of \$196 instead of the recommended \$168.<sup>1</sup> Their argument that the standard of living of the GP in Britain had declined under the system by about one-fifth, while that of all other occupations had risen by the same amount, persuaded the government, after several bitter months, to offer a compromise acceptable to the GP's.

The immediate commotion subsided but its initial provocation, the system of remuneration in Britain, still threatens government/physician relations. The GP's recommend a new NHS system. As one part of it they ask for direct reimbursement for expenses rather than the fixed annual amount of \$4,060 which is given to each doctor now, regardless of actual expenses.<sup>2</sup> A fixed amount encourages the GP's to spend sparingly and stay as far below this amount as possible, at the sacrifice of new and improved equipment, additional personnel and possibly good medicine.

Another change requested relates to the method of setting physicians' salary. The average GP salary is currently \$7,742 after expenses but before taxes (average income in Britain is slightly over \$2,000). This sum varies according to the number of patients a GP has on his list, which can range from 1,500 to 3,500 potential or actual patients, but averages about 2,300. The government pays a capitation fee of approximately \$2.87 to \$5.18 per patient each year, based on the cost of living, with various "loading" payments and allowances for "unpopular areas." The obvious complaint is that the GP's salary is unrelated to his work load, responsibility or quality of his work, except that a patient may elect to be on his lists. Physicians claim that about 1,500 patients is the maximum that can properly be attended, yet over half have more than 2,500 patients and 29 per cent more than 3,000.<sup>3</sup> A physician, therefore, who tries to offer conscientious care and personal attention to his patients must pay the price with a lower income. During an epidemic, or with a list of disproportionately older patients, one physician's work load will far exceed another's, though their incomes may remain equal.

The physicians, therefore, want the pool system of payment abolished in favor of fees for each item of work or straight salaries. The government has



thus far agreed to three conditions; provision of loans for improving practice conditions, reimbursement for office employees' salaries, and a reduction in required paper work.<sup>4</sup> No basic structural changes have yet been made.

Parenthetically, it should be noted that any physician in the British system may supplement his income with a private practice and that many do so. Although they do work harder, they are also better paid than most professionals in Britain. Lastly, despite their problems, the majority of the medical profession still is said to support emphatically a federally sponsored program of medical care.

#### MEXICO

Recent strife in Mexico inspired the whole medical profession to fight and some members to strike for an increase in pay for residents and interns. In many of the country's hospitals, most of which are run by government agencies, interns and residents are paid less than the minimum wage for unskilled labor, ranging from \$20 to \$148 per month in the Ministry of Health and \$32 for the first year to \$148 the fourth year in the Social Security Institute. The government, in addition, provides food, lodging, uniforms, and organizes teaching programs, which most students maintain are poorly organized. Young physicians want uniform raises to \$96 per month for interns and \$160 for residents with increments of \$40 monthly for each succeeding year up to a maximum of five years.<sup>5</sup>

The three-month strike concluded with the government yielding to all demands; a wage scale of \$120 to \$256 per month for interns and residents and a 10 per cent cost-of-living increment. It also agreed to improve living quarters, supply adequate work clothes and reorganize deficient teaching programs.

Whether this will be enough incentive to curb the shrinking enrollment of medical students remains to be seen. The AMM (Alianza de Medicos Mexicanos) contends that "medicine, which is largely socialized in Mexico, no longer attracts young men because of the low pay."<sup>6</sup>

#### SWITZERLAND

While Switzerland has no nationalized medical program, it does provide private sickness insurance funds whose representatives negotiate with the physicians to establish a scale of fees and procedures, insuring that doctors do not use extravagantly costly drugs or treatments. Difficulty arose recently when supervisory activities were assumed by the Fund administrators over the physicians and fees were held down. Swiss doctors were likewise angry because they had to work up to 80 hours per week, did not get paid holidays, had to pay their own expenses when in the service and received no pension.

The system is decentralized, allowing individual cantons to decide on compulsory or voluntary health insurance. Eighty to ninety per cent of the people are members of these private insurance associations.

The federal government subsidizes recognized private voluntary health plans, pays a fee-for-service and prescribes the conditions such associations have to meet to gain federal recognition. (Health insurance funds pay only a fraction of hospital expense, the rest being paid by the government.) These government-prescribed conditions primarily touch on questions of organizations, benefits, freedom of choice and relationship with the physician. The cantons are empowered to set fee schedules for compensation of doctors by the health plans, considering the arguments of both the medical profession and the insurance association. Fees are low, so doctors are able to make satisfactory incomes only by carrying heavy work loads, performing more technical and lucrative procedures (though they may be limited to specialists), and encouraging repeat visits to their offices. Recently the insurance association has tried to economize even further by holding down fees, and thus has caused the most recent difficulties.<sup>7</sup>

#### BELGIUM

One of the most widely publicized and intensely criticized and supported medical crises occurred in Belgium during the Spring of 1964. Physicians objected to a law passed by Parliament which awarded the government additional control over medical care, far more than the medical profession would agree to yield. While the conflict appeared to involve only a struggle for authority, a formidable objection lay in the inevitable cut in physician income which would result from the proposed measures. Physicians argued that the law "provided for a fixed schedule of fees to replace private fee arrangements between physician and patient . . . , would probably also result in higher taxes for doctors because fee receipts would give a central record of their incomes . . . , would turn independent physicians into civil servants; extend government control over the practice of medicine; restrict private practice to three half days a week; and violate the confidential relationship between doctor and patient." They complained of the threat to professional secrecy when patients were made to carry medical books and the threat to the doctor's right to give the treatment of his choice. The physicians demanded, and, with an 18-day strike, won, a guarantee of full control over the treatment of patients, free choice of physician by the patient and exemption of minor ailments from insurance coverage, to discourage unnecessary request.<sup>8</sup> They also received a raise in fee for surgery consultations, assurance that no schedule of fees would be effective without 60 per cent of the country's doctors contracting to work within the schedule, enough time for private practice and equal participation by doctors and members of the insurance organization on a National Committee.<sup>9</sup>

Belgium has had a compulsory health insurance scheme for workers below a certain income level since the end of the war, administered by several semi-official agencies attached to various trade unions and supported by members, employers, and government subsidies. The agencies decide the sums payable



to doctors on a fee-for-service basis and refund the patient about 75 per cent of this amount. However, there has been nothing to bind the physician to the standard agency rates, and most of them reportedly charged more without recording it, in order to avoid taxes on the extra amount. This scheme permitted physicians the full authority of a private practice and the security of patients and payments in a nationalized setting. The new law was intended to remove some of the authority—it only partly succeeded.<sup>10</sup>

#### ITALY

Italian physicians likewise tried to rectify what they felt was monetary injustice in an eight day strike in 1963. Officially, a hospital doctor's monthly basic salary may be as little as 43,000 lire (about \$70), although unofficial estimates place it at about 93,000 lire (or \$150) for juniors, excluding private work. The doctors demanded an official minimum (for those on salary, mostly specialists) of 150,000 lire (\$250).<sup>11</sup> Forty-five thousand physicians participated in the strike against low fees (for those on fee-for-service) and red tape in government-sponsored medicine. The government agreed to raise fees 40 per cent (though doctors on fee-for-service had requested a five-fold increase), to reduce paperwork and to standardize fees.<sup>12</sup>

Eighty per cent of all Italians are either compulsory or voluntary members of one of several state-subsidized insurance plans for medical and pharmaceutical payments. Some general practitioners are paid on a fee-for-service basis, other general practitioners by capitation and most specialists by salary. Provincial officers negotiate the type of payment.<sup>13</sup>

#### FRANCE

Doctors in Paris staged a one-day strike this Spring decrying the government's refusal to raise their fees. About 30,000 of the country's 37,000 family doctors refused to sign any administrative form, certificate, or social security documents. While the government admitted that such a fee increase would not be unreasonable (an official survey found the physician's income below that of butchers or bakers), it stalled a decision, maintaining that constant fees in recent years have not prevented doctors from increasing their incomes. They have simply been working harder (60-72 hours per week) under a fee-for-service program. The physicians claim they are overworked already. One solution has been to enter group practice, a phenomenon becoming almost as familiar to French as to British doctors.<sup>14</sup> The physicians, dissatisfied with a 3 per cent raise in the fee schedule (they had asked for a 13 per cent raise), have threatened to withdraw from the social security system by October of this year if the government does not increase medical fees. Concern now centers on whether the medical scheme will become a political issue which will result either in the scheme's complete dissolution or in its complete nationalization.<sup>15</sup> This remains to be seen.

The French system of medical care is government-sponsored, compulsory for employees, locally administered and also provides sick pay. It is handled through competing health insurance companies. The French patient must pay doctor, hospital and pharmacist himself and then file for reimbursement from the compulsory health plans. If his physician is a participant in the scheme, the patient is repaid 80-100 per cent of his bill. If not, he receives only 25 per cent. Cost of these plans is financed almost entirely by heavy social security taxes on both employee and employer.<sup>16</sup>

#### NEW ZEALAND

Hospital specialists in New Zealand warned their government that hospital lines would grow even longer and standards of care would be threatened if they did not do something about hospital salaries. They asked for removal of a salary scale that keeps a high proportion of full-time hospital specialists graded at a low level. Raises depend, the specialists complain, "on the vagaries of bureaucracy." The government has called a meeting to prepare recommendations on medical salaries, but nothing has yet been settled.<sup>17</sup>

New Zealand has two other systems of payment for general practitioners and specialists in independent practice: the "refund system," under which the doctor can charge the patient whatever fee he wants, but the patient can obtain from the social security authorities, on presentation of receipt, only his fee-for-service; and the "schedule" system, under which the physician bills directly to the social security authorities the amount in the schedule, but can ask for more than that from the patient. Hospital staff members, as in most countries, receive a salary. Medical services are available to everyone and are financed from the Social Security Fund. The patient can choose his doctor, and the doctor can choose his remuneration method.<sup>18</sup>

#### CANADA

In contrast with the above-mentioned cases, Canadian physicians, particularly those in Saskatchewan, following their bitter struggle with government three years ago, say their earnings have climbed considerably since the government plan was introduced, due to the increased volume of service, reduction of patients who are entitled to free service (e.g., ministers, fellow physicians, etc.) and negligible collection problems.<sup>19</sup> In fact, contrary to the trend in every other country mentioned, the number of practicing doctors in the province has climbed to about 1,000, or nearly 100 more than before the program was introduced a couple of years ago. Saskatchewan has North America's first universal government-sponsored medical insurance plan. For \$24 per family, every resident is completely covered against hospital and doctor bills. Private nonprofit agencies function in the administrative roles as a protection against government interference. Some physicians send their bills directly to the government, but most prefer



these collecting agencies or the patient himself. Regardless of which plan the patient selects—medical care plan, voluntary health insurance agency or neither—he is reimbursed up to 85 per cent of the schedule of minimum fees established by the Medical Care Commission.<sup>20</sup>

#### JAPAN

Discontent within the medical profession is mounting in Japan where physicians complain that they are the only professional group with a declining standard of living. Dissatisfaction with government handling of funds exists not only among physicians, but also among the debt-ridden health insurance organizations and the employee groups, all of whom object to a major rise in premium payments and the government's reluctance to subsidize chronic deficits. So far the discontent has been verbal only, allowing the government to remain recalcitrant on the issue.

Under a program adopted in 1961, about 99 per cent of Japan's citizens are covered by at least one of nine officially designated health insurance systems. The largest is the government-sponsored National Health Insurance Program, with a membership of approximately 45 million. Under the compulsory program, members pay a specified percentage of their incomes into a medical insurance program. Medical fees are rising and subsequent payment must come directly from the patient because the government refuses to pay.<sup>21</sup> Most governments contribute to this program as much as needed, having already collected it through income tax. The problem of who is going to suffer the losses in Japan as medical costs rise remains an open question.

## 2. Decline of Professional Status and Subsequent Authority of Physicians

While objections to this development are discreetly subdued, it is nevertheless fairly obvious that the physician's ego has suffered from what might be interpreted as diminution of status and transfer of functional role to that of a government functionary or worse, a clerk. The physician, in the most extreme cases of federal control, is no longer even the master in the practice of his own skills. This is made apparent when he is compelled to deliver control in medical matters into the hands of non-medical administrators, who neither understand nor sympathize with the problems of the physician.

Many American physicians have listed this inevitable and unacceptable government interference and control as the primary evil in the system. Examples of resistance to the distribution of authority are numerous. Strikers in Mexico asked that they be permitted to participate in the preparation of training programs. They demanded that medical personnel in government institutions be given the right to elect their directors, since politically appointed directors have often been unfair and unsympathetic to the medical staffs they supervise.<sup>22</sup> More equal dispersion of power is needed but is not feasible as long as the central government finances a substantial share of the expenditure. Doctors in almost all countries

are urgently asking that more administrative functions be transferred to them.

In Britain and other countries, the government not only regulates the maximum fees which the physician charges, but also controls and periodically checks the drugs administered and prescribed to insure that the physician has not intentionally selected unnecessarily expensive drugs. According to one embittered British physician, a doctor is fined for being too experimental in his treatment or for prescribing too many expensive drugs. Bureaucrats who know nothing about medicine decide what drugs are on the list. "Always the government exercises stringent control to cut costs and to do everything as cheaply as possible."<sup>23</sup> The result is that physicians tend to prescribe safe drugs, excluding the newer, and therefore more expensive drugs. This interference in drug dispersion ultimately gives government a voice in the physician's relationship to his patient and creates a paternal surveillance of his diagnoses when drugs are involved. The issue of drug regulation is still very controversial: while one side argues its importance to prevent overuse of unnecessarily expensive drugs when cheaper ones would do, the other side resents, as mentioned, the intimidation and interference in professional practices by laymen.

Not only has the physician in general suffered status decline in some countries, but federalized medicine has also had the effect of putting the GP in the shadow of the specialist. For example, while specialists in Britain have a government salary, full hospital privileges and limited control by the state, GP's earn considerably less without the security of a salary and regular hours, must struggle with the government in their less clearly defined and predictable practice and are deprived of hospital privileges and thus the right to follow their patient's progress. They complain about serving as a mere intermediary between patient and specialist, a middleman to refer the interesting cases on to the better qualified. The typical GP operates in a confined neighborhood, prescribes for trivial ailments, and funnels serious cases to specialists in hospitals; he is never entitled to remain with a case just because it interests him. He has none of the advantages of regular hours and regular holidays that are enjoyed by his colleagues in the specialties. GP's must work out arrangements for cover when they want to take any time off. The GP's in Britain revealed far more than just financial dissatisfaction in their united resistance this Spring. Along with low status and middleman functions, they complained of professional isolation, long working days, too many patients, the position of pariah in the eyes of half the men in their own profession, and the demand that they refer the simplest ailments to specialists.

The British GP's therefore want to be admitted into the community of medicine, to share in the hospital treatment of patients, to be given modern diagnostic aids, proper offices and staff, as the specialists.<sup>24</sup> They drew up a charter asking for a 5½



day week, overtime for evening and weekend work, six weeks holiday a year and direct repayment for expenses. They want to be able to choose between a flat salary, a fee per patient on the books, and a fee per item of service. So far the Ministry's only solution to the GP's isolation and excessive burden is to encourage group practice, thus giving the group a chance to work out a system for over-time and for holidays and to build specializations within the group.<sup>25</sup>

Physicians have worried a good deal about the depersonalization of the patient/doctor relationship as a result of their diminished control and status and having to treat too many patients. They argue that the patient must remain the central personage, but that he is in danger of losing this spotlight when doctors are paid by the fund rather than the patient. The patient is thus made passive in the transaction and completely unaware of the pressure exerted on doctors by the fund. Part of the Canadian problem dealt with what the doctors feared would be a dissolution of this special relationship with the current overflowing of doctor's offices and unnecessary use of facilities. In 1962, Saskatchewan physicians won world-wide attention in a 23-day strike protesting the government's denial of their participation in the design and approval of a comprehensive medical plan which gave the Premier almost total decision-making power over the type of medical plan, terms and conditions of physicians' services, payment, and other points. The government refused to amend the act, so they struck, not by refusing to provide care, but by providing free service. Public outcry forced the government to capitulate, and physicians completely revised the act. Fearing government control and supervision if forced to take money directly from it, they insisted on the continuation of voluntary nonprofit administering agencies as the intermediary agent, both as a face-saving device and a buffer against government. They also demanded private practice privileges and private voluntary programs to provide for both themselves and their patients the opportunity for freedom of choice. Only about 10 per cent of the physicians receive direct reimbursement from the government today.<sup>26</sup> While they admitted the necessity of some policing, the physicians asked that they be allowed to do their own, through the College of Physicians and Surgeons, which should have the further responsibility of licensing doctors, setting their fees and disciplining them.<sup>27</sup>

Although many feel that government control threatens the doctor/patient relationship, some physicians claim that nationalized programs have actually improved this relationship. They insist that while the physician cannot give each patient as much time as he would like, he is able to offer better and more complete treatment and is bothered by fewer hypochondriacs.<sup>28</sup> Some insist that the doctor/patient relationship is improved because the element of cost is removed.

### 3. Dominance of Political Decisions in Allotting Funds

One of the most serious difficulties that emerges in almost any nationalized medical program is the inevitable conflict between two groups both dependent on the same limited resources to fulfill their functions. This is the delicate balance and struggle between the Ministry of Finance (or equivalent) and the medical profession, over the exhaustible resource—the budget. The obvious advantage, by virtue of both control and proximity, belongs to the Ministry and it is the use of this advantage which has in the past forced the medical profession into dramatic actions of resistance. While the Ministry concentrates on balancing the budget with its own set of weights and measures, the medical field often suffers because medical expenses necessarily rise with a growing population, a larger elderly group, a higher standard of living, and new technology. As the Ministry weighs one national need against another, one pressure group against another, it is not surprising that the decisions have created severe shortages in the medical field. Annual budgets have been cut in financial crises in a way that is not compatible with good medicine. A shortage of hospitals and professional medicine men plagues almost every program. This is particularly true in Britain, where not one hospital was built for the first 15 years of the program, finally forcing the government to recently embark on a crash program of construction and rejuvenation. Long waiting lists appear on the records of all hospitals with sometimes as long as a year wait before patients can be admitted for elective procedures. Research fell far behind the United States and other countries and doctors were and are immigrating at about 500 per year to the United States and Canada where salaries are much higher. Almost one-half of 3,100 hospitals are operated by the NHS, but only five of these have been completed since the end of World War II. Two-thirds of the hospitals were built before the turn of the century.<sup>29</sup> The cost of the NHS in 1960 was 3.8 per cent of the value of all goods and services produced in Britain—at least a third less than the comparable cost of U.S. medical care that year and would have been still less if Americans could afford all the medical care they want.<sup>30</sup>

Likewise the shortage of physicians in Britain is still so severe that almost half of the emergency surgery is done by non-British trained doctors, primarily from India, whence a major portion of Britain's present medical staff originate. The number of students in training at present is below the 1938 level, a fact of considerable concern to the medical profession and the government. As Britain solves its doctor shortage with Indians, the Indian government is finding itself in the same predicament. Last year alone they had 3,000 vacant posts with pay so low and institutional facilities so limited that the Indians elected to immigrate to Britain. They complain that the Indian government demands and expects a "spirit of self-sacrifice," primarily monetary. In desperation



the government has clamped down on passport and foreign currency issuance to medical men.<sup>31</sup>

Many critics of socialized medicine protest the removal of medical care from a competitive market. British Professor D. S. Lees, a noted adversary of NHS, feels that medical care should be open to experimentation and innovation, that a tax-financed monolithic structure is "ill-suited to a service in which the personal element is so strong, in which rapid advancement in knowledge require flexibility and freedom to experiment, and for which consumer demands can be expected to increase with growing prosperity."<sup>32</sup> He maintains that "The fundamental weaknesses of NHS are the dominance of political decisions, the absence of built-in forces making for improvement and the removal of the test of the market."<sup>33</sup>

There is the possibility that, because NHS and many other federally sponsored programs of medical care are complete monopolies, innovation need not be encouraged and may even be curbed. With the absence of substitutes there are no strong external forces to encourage improvements in quality and efficiency. Economy can be stressed at the expense of better hospitals and equipment, better paid physicians, and the latest drugs and medical research, all of which represent increasing costs (and needs) in any program of public medicine.

#### 4. Bureaucracy of Federal Control

Federal control usually entails a raft of paper work, much of which has been cut down or controlled, but which still remains an issue in evaluating a government program of medical care. Some "red tape" is inevitable and results in delays in answering requests, complicated and impersonal channels of communication and the general clumsiness of a giant operation. Some physicians claim that they have had to hire a clerk just to handle the administrative aspects of patient care.

#### 5. The Patient's Perspective: Impersonality of Care

While the patients of those countries with nationalized medical care generally support their program with its attendant security and economy, they nevertheless find fault with the long waits necessary both at the hospital and in doctors' offices. When one finally does see a physician, they protest, his visit must be brief in view of the long line still waiting. The sheer magnitude of the patient rolls prohibits a doctor from providing the amount of personal care and attention which both parties desire. His role must necessarily be confined to that of a professional, no longer identified as friend and confidant in the fashion traditional for physicians.

It has been suggested that many people continue to seek private treatment, in programs where the alternative is given, because they resent having to wait hours for consultation and prefer calling for an appointment, they do not like being put in a ward of 20 or 30 patients with only screens for privacy, and they do not like being used as subjects for

the training and teaching of medical students.<sup>34</sup> Patients, feeling a loss of personal attention to their needs complain that there is a minimum which the doctor must perform and that few go beyond this.

The fact that criticism and complaints alone have been stressed in this paper does not mean that they outweigh the amount of praise and success accorded these programs. It has been intimated already that the problems herein discussed are all rectifiable and very few of those complaining suggest that the system itself be abolished. On the contrary, the establishment of a closer liaison between the government-controlled administering agencies and the medical profession has resulted from the necessity of each to recognize, deal with and try to alleviate the problems, difficulties, pressures and needs of each of the two bodies. Greater sympathy, understanding and teamwork are emerging from the struggles of these conflicting interest groups, who, together, must shoulder the responsibility for the nation's medical care.

Many do think, however, that there should be a simultaneously operated private system (as exists in several countries now) to offer an opportunity for choice. This would provide a necessary incentive and stimulus for improvement and progress in the profession. In Britain a program has been requested where people can contract out, pay less in contributions and use the money saved to pay for their own doctor and other medical services. As the system stands now, any patient can pick any doctor under either private or public arrangement, but all must still contribute to NHS, so they would in effect pay twice if they desired private care. Many countries have compulsory insurance for certain income groups, above which the individuals have the option of remaining in the program or leaving it in favor of a private insurance program or none at all, at which time they need pay no longer for the federal program. This system has the dual feature of providing and insuring medical security for those unable to afford it alone, and free choice in the medical market for those who can afford it. Physicians also can combine the best elements of both programs.

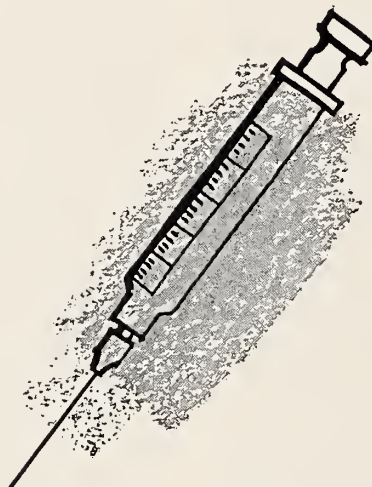
As indicated in the introduction, this Report has attempted to outline some of the problems encountered under nationalized health programs. Insight into their causes may enable policy-makers in the United States to avoid the pitfalls which have created these problems and permit them to implement recently enacted legislation more efficiently.

693 Sutter Street, San Francisco, California 94102.

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# NEWS & NOTES

NATIONAL • STATE • COUNTY

## LOS ANGELES

The William S. Middleton Award, the Veterans Administration's highest honor for medical research, has been presented to Dr. Lucien B. Guze and Dr. George M. Kalmanson of the Veterans Administration Center in Los Angeles.

Drs. Guze and Kalmanson have isolated a bacterial form, protoplast, from animals with pyelonephritis. The presence of this bacterial form offers an explanation for the unaccounted persistence and progression of kidney infections in the absence of the usual bacterial.

## SACRAMENTO

The Sacramento Medical Society has announced the following list of officers for 1966: President, Dr. Orrin S. Cook, succeeding Dr. Donald P. Hause; president-elect, Dr. James W. Martin; secretary, Dr. Pierce A. Rooney, Jr.; treasurer, Dr. James O. Farley.

## SAN FRANCISCO

Dr. Abraham M. Rudolph has been appointed Professor of Pediatrics, School of Medicine, University of California, San Francisco. The appointment becomes effective 1 July. Since 1960 Dr. Rudolph has been Professor of Pediatrics, Associate Professor of Physiology and Director of Pediatric Cardiology at Albert Einstein College of Medicine, New York.

\* \* \*

Dr. William F. Hoyt, Associate Professor of Ophthalmology, School of Medicine, University of California San Francisco Medical Center, is the recipient of an award given by the Heed Ophthalmic Foundation. Presentation was made at the annual convention of the Academy of Ophthalmology and Otolaryngology held recently in Chicago. Dr. Hoyt was selected because of his contributions to teaching and research in 1965.

The Heed Ophthalmic Foundation is a private foundation that has supported fellowships in ophthalmology since the late 1940's.

## SANTA BARBARA

The American College of Physicians will hold a regional meeting for internal medicine specialists in Southern California, in Santa Barbara, 18, 19 and 20 February.

The three-day scientific meeting will be held at the Biltmore Hotel. It will consist of scientific presentations, informal luncheons and an evening banquet Saturday.

Guests will include Dr. Irving S. Wright, New York, ACP president-elect and professor of Clinical Medicine at Cornell Medical College, who will address the internists 19 February on "The Modern Treatment of Stroke"; Dr. Edward C. Rosenow, Philadelphia, ACP executive director, and Dr. George C. Griffith, Los Angeles, ACP regent and emeritus professor of Medicine, University of Southern California.

The meeting is under the direction of Dr. W. Philip Corr, Sr., ACP governor for Southern California and clinical professor of medicine, Loma Linda University. Dr. Edward W. Boland, Los Angeles, is general chairman, and Drs. J. Edward Berk, Los Angeles, and Thurman K. Hill, Santa Barbara, are chairmen of the program and local arrangements committees, respectively.

A recall of a half million disposable hypodermic needles, down to the physician and user level, was announced recently by Commissioner James L. Goddard of the Food and Drug Administration.

Physicians, clinics and hospitals are warned not to use "Jintan Hyposterile Disposable Needles" or "Jintan Hyposterile Disposable Blood Needles" distributed by the Hypo Surgical Supply Corporation of New York City.

Dr. Goddard said that 13 of the 49 samples examined contained nonsterile needles. Other lots were found containing packages in which the sealing had come loose, exposing them to airborne contamination.

Nonsterility of the needles was reported in December 1965 by the New York City Health Department and the New Jersey State Health Department. Data from FDA's sterility test confirmed the findings.

Hypo Surgical Supply has sent telegrams to all of its jobbers and wholesalers requesting the recall of the needles down to the user level. The needles have been distributed throughout the country.

## SANTA CLARA

Dr. Malcolm M. Merrill has received the first Palo Alto Medical Research Foundation \$5,000 Public Health Service Award.

Dr. Merrill, formerly California State Director of Public Health, is now chief of Health Services in the Office of Technical Cooperation and Research in the United States Department of State.

The Foundation's Public Health Service Award was established by a \$5,000 gift to the Foundation by an anonymous donor. The gift was made with the stipulation that it be used, "to encourage outstanding and dedicated service in the field of public health in California by making an honorary cash award to a doctor who has distinguished himself in this important field of medicine."

## GENERAL

Opening of a contest among physicians to deliver a memorial lecture dedicated to the late Harold G. Wolff, M.D., Cornell neurologist, was announced recently by Dr. Donald J. Dalessio of La Jolla, on behalf of the American Association for the Study of Headache.

Dr. Dalessio, editor of *Headache*, the association's journal, said that the winning entry will receive an award of \$1,000, and will be selected on the basis of reflecting most closely "the pioneering spirit in which Dr. Wolff approached basic and clinical research on pain and headache."

The award, which is to be made annually hereafter, will be for the "best original paper on headache, head pain, or on the nature of pain itself." The paper may be concerned with basic research, clinical studies, or both. All physicians, including those in training as fellows or residents, are eligible.

Author of the winning paper will be invited to read his paper at the annual meeting of the Association which this year will be held in Chicago on 25 June. The deadline for submission of papers is 15 May. They should be mailed in duplicate to Dr. Dalessio at 8878 Nottingham, La Jolla, Calif. Nonwinning papers may be published in *Headache*, or authors may be asked to deliver them at the annual meeting.

# EDUCATION NOTICES

## Meetings and Courses

### COMMITTEE ON CONTINUING MEDICAL EDUCATION

THIS BULLETIN of the dates of continuing education programs and the meetings of various medical organizations in California is supplied by the Committee on Continuing Medical Education of the California Medical Association. In order that they may be listed here, please send communications relating to your future meetings or postgraduate courses to Committee on Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco, California 94102.

#### KEY TO ABBREVIATIONS AND SYMBOLS

##### Medical Centers and CMA Contacts for Postgraduate Course Information

<b>CMA:</b>	<b>California Medical Association</b> For information contact: Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco 94102. PROspect 6-9400, Ext. 68.
<b>LLU:</b>	<b>Loma Linda University</b> For information contact: W. F. Norwood, Ph.D., Associate Dean, Continuing Education, Loma Linda University School of Medicine, 1720 Brooklyn Ave., Los Angeles 90033, ANgeles 9-7241, Ext. 214.
<b>PRES. MED. CTR.</b>	<b>Presbyterian Medical Center</b> For information contact: Arthur Selzer, M.D., chairman, Education Committee, Presbyterian Medical Center, Clay and Webster Streets, San Francisco 94115, WEst 1-8000.
<b>UCLA:</b>	<b>University of California at Los Angeles</b> For information contact: Donald Brayton, M.D., Assistant Dean for Postgraduate Medical Education, 15-39 Rehabilitation Center, University of California Center for Health Sciences, Los Angeles 90024, 478-9711, Ext. 4345.
<b>UCSF:</b>	<b>University of California, San Francisco</b> For information contact: Seymour M. Farber, M.D., Dean, Educational Services and Director, Continuing Education, University of California Medical Center, Room 565-U, San Francisco 94122, 666-1692.
<b>USC:</b>	<b>University of Southern California</b> For information contact: Phil R. Manning, M.D., Associate Dean, Postgraduate Division, USC School of Medicine, 2025 Zonal Ave., Los Angeles 90033, CApital 5-1511, Ext. 300.
<b>STAN:</b>	<b>Stanford University</b> For information contact: Roy Cohn, M.D., Associate Dean for Graduate Affairs, Stanford University School of Medicine, 300 Pasteur Drive, Palo Alto, DAVenport 1-1200.

### FEBRUARY

- February 16-20—**Controversial Areas in Surgery.** UCLA at Palm Springs. Wednesday-Sunday.
- February 18-19—**Pediatric Dermatology.** UCSF. Friday-Saturday. 11½ hours. \$40.
- February 18-20—**American College of Physicians Southern California Regional Meeting.** Biltmore Hotel, Santa Barbara. Friday-Sunday. Contact: W. Philip Corr, M.D., governor, 3660 Arlington Avenue, Riverside 92506.
- February 19-20—**Neuropsychiatry in Daily Practice.** UCSF at Monterey County Hospital, Salinas. Saturday-Sunday. 9 hours. \$10.
- February 20-23—**Current Concepts in Chemotherapy.** UCLA at Palm Springs. Sunday-Wednesday.
- February 24-25—**Medical-Surgical Gastroenterology Conference.** USC. Thursday-Friday.
- February 25—**Annual Sterling Bunnell Memorial Lecture on Reconstructive Surgery.** Lane Hall, Pres. Med. Ctr. Friday. 8:00 p.m. Contact: Donald R. Pratt, M.D., chairman, 516 Sutter Street, San Francisco 94102.
- February 25-26—**Workshop on Hand Injuries.** Pres. Med. Ctr. Friday-Saturday. 12 hours. \$75.
- February 25-27—**Conference on Mental Retardation for Physicians.** UCSF. Friday-Sunday. 13½ hours. \$20.
- February 27-March 2—**Surgical Applied Anatomy.** LLU. Sunday-Wednesday. 29½ hours. \$100.

### MARCH

- March 2-3—**Los Angeles County Heart Association Annual Spring Symposium.** Statler Hilton Hotel, Los Angeles. Wednesday-Thursday. 12 hours. Contact: Professional Symposium Committee, LACHA, 2405 W. Eighth Street, Los Angeles 90057.
- March 2-3—**Western Electroencephalography Society Annual Meeting.** Hilton Hotel, San Francisco. Wednesday-Thursday. Contact: Edward E. Shev, M.D., secretary treasurer, 516 Sutter Street, San Francisco.
- March 2-4—**American Medical Association Air Pollution Medical Research Conference.** Ambassador Hotel, Los Angeles. Wednesday-Friday. Contact: Air Pollution Medical Research Conference, Department of Environmental Health, AMA, 535 N. Dearborn Street, Chicago, Illinois 60610.
- March 3-4—**Symposium on Diabetes.** USC at the Ambassador Hotel, Los Angeles. Thursday-Friday. 14 hours.
- March 3-6—**The Federation of Western Societies of Neurological Science.** Hilton Hotel, San Francisco. Thursday-Sunday. Contact: Robert B. Aird, M.D., chairman, Program Committee, FWSNS, Department of Neurology, University of California School of Medicine, San Francisco 94122.
- March 4-5—**Gynecology for the Non-Gynecologist.** UCSF. Friday-Saturday. 10¼ hours. \$40.
- March 4-5—**Operable Heart Disease.** Pres. Med. Ctr. Friday-Saturday. 16 hours. \$35.
- March 5-6—**Techniques in Surgery of the Knee.** UCLA. Saturday-Sunday. 12 hours. \$65.



March 5-6—**Sex Education and the Family Doctor.** UCSF at Herrick Hospital, Berkeley. Saturday-Sunday. 12 hours. \$15.

March 9-11—**Conference on Keratoplasty.** Pres. Med. Ctr. Wednesday-Friday. 21 hours. \$125. Contact: Lions Eye Foundation, Pres. Med. Ctr., 2018 Webster Street, San Francisco 94115.

March 9-13—**Diagnostic Radiology.** UCSF. Wednesday-Sunday. 28¼ hours. \$110.

March 10—**Symposium on Obesity.** USC at the Ambassador Hotel, Los Angeles. Thursday. 7 hours.

March 10-14—**Pulmonary Problems.** UCLA. Thursday-Sunday.

March 11-12—**Childrens Hospital Medical Center Annual Postgraduate Seminar and Clifford D. Sweet Lecture.** Childrens Hospital, 51st and Grove Streets, Oakland. Friday-Saturday. 16 hours. \$30 for 4 sessions or \$10 per session. Contact: Miss Inetta Carty, Medical Staff Office. Childrens Hospital Medical Center, Oakland.

March 11-12—**WEST COAST COUNTIES—Regional Postgraduate Institute presented by California Medical Association** in cooperation with UCSF. Ojai Valley Inn, Ojai. Friday-Saturday. \$15. "Indications for Surgical Intervention—The Difficult Decision." Chairman: George J. Wittenstein, M.D., 2235 Castillo, Santa Barbara.

March 12—**Cancer: Childhood and Adult Tumors.** UCSF at Childrens Hospital and Adult Medical Center, San Francisco. Saturday. 7¼ hours. \$15.

March 12—**Obstetrics and Gynecology.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

March 12-13—**Neuropsychiatry in Daily Practice.** UCSF at Agnews State Hospital, San Jose. Saturday-Sunday. 12 hours. \$10.

March 13-17—**Alumni Postgraduate Convention, LLU.** March 13-14 (Sunday-Monday)—Refresher Courses. White Memorial Medical Center. March 15-17 (Tuesday-Thursday)—Scientific Assembly. Ambassador Hotel, Los Angeles. Contact: Samuel H. Fritz, M.D., general chairman, 1832 E. Michigan Avenue, Los Angeles 90033.

March 13-April 11—**Medical Centers of Egypt, Jordan, Lebanon, Turkey, Greece and Italy.** Sponsored by USC. 39 hours. \$200.

March 16—**Annual Postgraduate Symposium on Heart Disease.** O'Connor Hospital, San Jose. Wednesday. \$15., incl. lunch. Contact: William G. Allayaud, executive director, Santa Clara County Heart Association, 1961 The Alameda, San Jose 95126.

March 16—**Symposium on Obesity.** USC. Wednesday.

March 19—**Catecholamines and Adrenergic Blocking Agents.** Sponsored by the American College of Cardiology and USC. Ambassador Hotel, Los Angeles. Saturday. Members: \$20., Non-Members: \$25. Contact: Executive Director, ACC, 9650 Rockville Pike, Washington, D.C. 20014.

March 19—**American College of Chest Physicians California Chapter Annual Meeting.** Biltmore Hotel, Los Angeles. Saturday. 9:00 a.m.-5:00 p.m. Contact: M. Rosenblatt, M.D., program chairman, County of Los Angeles Health Department, 220 North Broadway, Los Angeles 90012.

March 19—**Rheumatic Diseases: Diagnosis and Treatment.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

March 19-20—**California Radiological Society Annual Meeting.** Biltmore Hotel, Los Angeles. Saturday-Sunday. Contact: L. H. Garland, M.D., 450 Sutter Street, San Francisco.

March 20-23—**CALIFORNIA MEDICAL ASSOCIATION 95th Annual Session.** Scientific theme: "CURRENT CONCEPTS IN THERAPY: Coronary Artery Disease. Gastrointestinal Hemorrhage. Renal Failure." Biltmore Hotel, Los Angeles. Sunday-Wednesday. Contact: California Medical Association, 693 Sutter Street, San Francisco 94102.

March 25-27—**Postgraduate Assembly in Anesthesiology.** Sponsored by the Anesthesia Section, Los Angeles County Medical Association. International Hotel, Los Angeles. Friday-Sunday. 12 hours. \$25. Contact: Thomas W. McIntosh, M.D., secretary, Postgraduate Committee, 686 East Union Street, Pasadena.

March 26—**Endocrinology.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

March 26-27—**Sex Problems in Clinical Practice: The Critical years.** UCSF. Saturday-Sunday. 12¾ hours. \$40.

March 29-30—**Southwestern Pediatric Society.** Statler Hilton Hotel, Los Angeles. Tuesday-Wednesday. Contact: Phillip Sturgeon, M.D., 1200 S. Vermont Avenue, Los Angeles 90006.

#### APRIL

April 1—**Fresno County Heart Association Annual Physicians Cardiovascular Symposium.** Hacienda Hotel, Fresno. Friday. \$15. Contact: Roger K. Larson, M.D., chairman, Professional Symposium Committee, FCHA, 1759 Fulton Street, Fresno.

April 1-2—**Contrast Media in Abdominal Disease: A Program for the Practicing Physician.** UCSF. Friday-Saturday.

April 1-2—**Joint Manipulations in Perspective.** UCSF. Friday-Saturday.

April 1-2—**Annual Symposium on the Newborn.** Sponsored by the Pediatric Department, Southern California Permanente Medical Group, and Kaiser Foundation Hospitals. International Hotel, Los Angeles. Friday-Saturday. Contact: Shirley Gach, Room 3011, 4900 Sunset Blvd., Los Angeles 90027.

April 4-8—**Mental Retardation Institute.** USC. Monday-Friday.

April 5-8—**American Association of Anatomists.** San Francisco Hilton, San Francisco. Tuesday-Friday. Contact: Russell T. Woodburne, executive secretary, The University of Michigan East Medical Bldg., Ann Arbor, Michigan 48104.

April 6-27—**Advanced Funduscopy.** USC. Wednesdays.

April 6-May 11—**Psychiatry in General Practice.** UCSF at Stockton State Hospital, Stockton. Wednesdays.

April 7-June 9—**Ward Walks in Rare Diseases.** USC. Thursdays.

April 12-June 14—**Bedside Cardiology.** USC at St. Vincent's Hospital. Tuesdays.

April 13-15—**The Pacific Regional National Rehabilitation Association Conference.** Sheraton-Palace Ho-

tel, San Francisco. Wednesday-Friday. \$12., including keynote luncheon. Contact: Tak Taketa, chairman, Publicity Committee, 1111 Jackson Street, Rm. 5040, Oakland 94607.

April 13-16—**American Orthopsychiatric Association.** San Francisco Hilton, San Francisco. Wednesday-Saturday. Contact: Marion F. Langer, Ph.D., executive secretary, 1790 Broadway, New York 10019.

April 14-16—**Retinal Detachment Conference.** Lions Eye Bank. Thursday-Saturday. 8 hours. \$100. Contact: Eva del Oro, secretary, Lions Eye Bank, 2018 Webster Street, San Francisco.

April 16—**Ankle Injuries in Athletics.** UCLA. Saturday. 6 hours. \$25.

April 16-17—**The Uncertain Quest: The Teen-Ager's World.** UCSF. Saturday-Sunday.

April 21-23—**Endocrinology and Metabolism.** UCSF. Thursday-Saturday.

April 23-24—**Neuropsychiatry for the Non-Psychiatric Physician in General Practice.** UCSF at Sutter Memorial Hospital, Sacramento. Saturday-Sunday.

April 25-27—**Annual Meeting of the Council on Medical Television.** UCSF. Monday-Wednesday. Contact: Irving Merrill, M.D., director, Office of Television Research, UCSF.

April 28-29—**General Surgery.** UCSF. Thursday-Friday.

April 28-29—**Symposium on Hypertension.** USC. Thursday-Friday.

April 29-May 1—**REDWOOD REGIONAL CONFERENCE** presented by California Medical Association in cooperation with USC. Konocti Harbor Inn, Clear Lake. Friday-Sunday. \$15. "Cardiovascular Disease, Endocrinology, Office Techniques in Patient Interviews." Chairman: Lucius L. Button, M.D., 1102 Montgomery Drive, Santa Rosa.

## MAY

May 1-5—**American Society for Microbiology.** Biltmore Statler Hilton Hotel, Los Angeles. Sunday-Thursday. Contact: R. W. Sarber, executive secretary, 115 Huron View Blvd., Ann Arbor, Michigan.

May 5-7—**Ear, Nose, Throat.** UCSF. Thursday-Saturday.

May 5-26—**Neuropsychiatric Management in Daily Practice.** UCSF at Modesto State Hospital, Modesto. Thursdays.

May 6-7—**Obesity.** UCSF. Friday-Saturday.

May 7—**Ventura County General Hospital Annual Staff Seminar.** VCGH. Saturday. 6 hours. No fee. Contact: G. K. Ridge, M.D., VCGH, 291 Loma Vista Road, Ventura.

May 7-8—**Dynamic Measurements with Radioisotope Techniques for Evaluating Organ Function and Circulation.** UCLA. Saturday-Sunday.

May 11—**American Cancer Society Scientific Session.** St. Francis Hotel, San Francisco. Wednesday. Contact: Lewis W. Guiss, M.D., 1930 Wilshire Blvd., Los Angeles 90057.

May 12-15—**Hawaii Medical Association Annual Meeting.** Arthritis and Psychiatry. Princess Kaiulani Hotel, Honolulu. Thursday-Sunday. 15 hours. \$35. Contact:

Miss Lee McCaslin, executive secretary, 510 S. Bereania, Honolulu, Hawaii 96813.

May 13-14—**Convulsive Disorders.** UCSF. Friday-Saturday.

May 13-14—**SAN JOAQUIN VALLEY COUNTIES—Regional Postgraduate Institute** presented by California Medical Association in cooperation with UCLA. Ahwahnee Hotel, Yosemite. Friday-Saturday. \$15. "Cerebral and other Peripheral Vascular Disease, Headache. Chairman: Dale Kirkegaard, M.D., 2432 Calaveras Street, Fresno.

May 14—**Humboldt-Del Norte Medical Society Annual Medical Symposium: "Frontiers in Medicine."** Eureka Inn, Eureka. Saturday. 4 hours. Contact: Stanwood S. Schmidt, M.D., president, 707 K Street, Eureka.

May 14-15—**Hypnosis, A Critical Evaluation.** UCSF at Napa State Hospital, Imola. Saturday-Sunday.

May 19—**California Heart Association Annual Scientific Session.** Ambassador Hotel, Los Angeles. Thursday. 6 hours. No fee. Contact: Arthur Feinfeld, M.D., CHA, 1370 Mission Street, San Francisco.

May 20-21—**San Diego Academy of General Practice Annual Postgraduate Symposium** presented in cooperation with University of Oregon School of Medicine. Vacation Village Hotel, Mission Bay, San Diego. Friday-Saturday. Contact: Orlando P. Johann, M.D. 731 E. Broadway, El Cajon.

May 20-22—**Complications in Modern Medical Practice.** UCLA. Friday-Sunday. 18 hours.

May 21—"Clinic Day"—**Diseases of Medical Progress.** Channing House Auditorium, Palo Alto. Saturday. 9:00 a.m. to 3:30 p.m. Contact: R. Hewlett Lee, M.D., Palo Alto Medical Clinic, 300 Homer, Palo Alto.

May 21-22—**Health of the School Child.** UCSF. Saturday-Sunday.

May 23-25—**American Thoracic Society Annual Meeting.** Hilton Hotel, San Francisco. Monday-Wednesday. Contact: James Kieran, M.D., chairman, Medical Sessions Committee, American Thoracic Society, 1790 Broadway, New York, N.Y. 10019.

May 28-June 29—**Medical Centers of Europe.** USC. 50 hours. \$250.

May 20-21—**San Diego Academy of General Practice Annual Postgraduate Symposium** in cooperation with University of Oregon School of Medicine. Vacation Village Hotel, Mission Bay, San Diego. Friday-Saturday. Contact: Orlando P. Johann, M.D., 731 E. Broadway, El Cajon.

## JUNE

June 11-12—**The Drug Takers.** UCLA. Saturday-Sunday. 12 hours.

June 16-19—**California Society of Anesthesiologists Biennial Scientific Meeting.** Sahara Tahoe Hotel, South Shore, Lake Tahoe. Thursday-Sunday. \$25. Contact: Mr. Norman R. Catron, executive secretary, CSA, 39 North San Mateo Drive, San Mateo 94401.

June 17—**Attending Staff Association of Olive View Hospital Symposium on Infectious Diseases.** OVH, Olive View. Friday. Contact: Joseph K. Indenbaum, M.D., secretary-treasurer, ASAOVH, Olive View.



June 22-24—**Highlights of Modern Ophthalmology.** Lions Eye Bank. Wednesday-Friday. 8 hours daily. \$75. Contact: Eva del Oro, secretary, Lions Eye Bank, 2018 Webster Street, San Francisco.

June 22-24—**Treatment of Fractures.** USC. Wednesday-Friday.

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**USC:**

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TO HAVE YOUR MEETING OR PROGRAM LISTED IN CALIFORNIA MEDICINE

**FILL OUT AND MAIL THIS BLANK TO THE ADDRESS GIVEN**

(COPY MUST BE **RECEIVED** NOT LATER THAN THE **FIFTH OF THE MONTH PRECEDING** ISSUE)

**Continuing Medical Education, California Medical Association**

693 Sutter Street, San Francisco, California 94102

NAME OF ORGANIZATION\_\_\_\_\_

MEETING OR PROGRAM\_\_\_\_\_

DATE\_\_\_\_\_TIME\_\_\_\_\_

PLACE\_\_\_\_\_FEE, IF ANY\_\_\_\_\_

CONTACT FOR INFORMATION:\_\_\_\_\_  
(give name, title, address)



## The Physician's BOOKSHELF

**TEXTBOOK OF OBSTETRICS**—John C. Ullery, M.D., Chairman and Professor of Obstetrics and Gynecology, The Ohio State University College of Medicine, Columbus, Ohio; and Zeph J. R. Hollenbeck, M.D., Professor of Obstetrics and Gynecology, The Ohio State University College of Medicine, Columbus, Ohio, and thirty-one contributors. Foreword by Richard L. Meiling, M.D., Dean, The Ohio State University College of Medicine, Columbus, Ohio. The C. V. Mosby Company, St. Louis, 1965. 752 pages, \$17.50.

"Textbook of Obstetrics" represents the efforts of the teaching staff of the Department of Obstetrics and Gynecology at Ohio State University College of Medicine to describe the proper management of the pregnant patient from conception through involution. This is accomplished by 33 different authors in 57 chapters and 729 pages, and while such multiple authorship allows authoritative omission, there is an excess of fragmentation and repetition of subject matter.

The contents are presented in a sequential pattern. The topics, however, are discussed in a superficial and casual manner with minimal efforts to support recommendations with either data or references. The text, then, is neither a standard reference source nor, because of its length, a synopsis. While it is disappointing to find in a 1965 publication so little detailed discussion of recent developments in obstetrics, for an obstetrical text, it does discuss an unusually wide range of medical topics.

Most of the illustrations appear to be original and while only three are in color, they are adequate. For those interested in learning the general philosophy and specific methods used at the Ohio State University College of Medicine, the book is of obvious value. For others, one of the synopsis or standard obstetrical texts currently available would seem to be a better buy.

R. C. GOODLIN, M.D.

**DISEASES OF THE NEWBORN—Second Edition**—Alexander J. Schaffer, M.D., Associate Professor of Pediatrics, The Johns Hopkins Medical School, and Pediatrician to The Johns Hopkins Hospital; Formerly Pediatrician-in-Chief, at present Attending Pediatrician to The Sinai Hospital of Baltimore, Maryland; Chief of Pediatrics (Nursery Service), The Hospital for the Women of Maryland; Director, The Johns Hopkins Community Pediatric Program. With a Section on Neonatal Cardiology by Milton Markowitz, M.D., and a Section on Fluid & Electrolyte Therapy by Lawrence Finberg, M.D. W. B. Saunders Company, Philadelphia, 1965. 1023 pages, \$22.00.

This is the second edition of what probably has become the most widely used comprehensive text on the newborn. Errors in the first edition have been largely corrected, omissions such as a discussion of the tetany of the newborn have been added, and such rapidly expanding fields as chromosomal abnormalities, inborn errors of metabolism and newborn immunology have been updated. The section on cardiovascular disorders by Markowitz has been rewritten and a new one on fluid and electrolyte balance by L. Finberg has been added.

The book remains a recommended one for neonatologists, obstetricians, pediatricians and general practitioners who desire a practical text on newborn care.

**PHYSICAL EXAMINATION OF THE JOINTS**—William P. Beetham, Jr., M.D., A.A.C.P., Former Fellow in Medicine; Mayo Graduate School of Medicine, University of Minnesota; Howard F. Polley, M.D., M.S. in Medicine, F.A.C.P., Head of a Section of Medicine (Rheumatic Diseases), Mayo Clinic; Professor of Medicine, Mayo Graduate School of Medicine, University of Minnesota; Charles H. Slocomb, M.D., M.S. in Pathology, Senior Consultant in a Section of Medicine (Rheumatic Diseases), Mayo Clinic; Professor of Medicine, Mayo Graduate School of Medicine, University of Minnesota; and Walt F. Weaver, M.D., M.S. in Medicine, A.A.C.P., Former Fellow in Medicine, Mayo Graduate School of Medicine, University of Minnesota, Rochester, Minn. W. B. Saunders Company, Philadelphia and London, 1965. 198 pages, \$7.50.

This book sets forth an excellent basic plan of attack for all beginners of joint examinations and a very useful refresher for the mature physician not only in general medicine but also in Orthopedic Surgery and Rheumatology. It is well organized, giving anatomical descriptions of all the joints followed by techniques of examination including inspection, palpation, movement and range of motion plus added excerpts for special areas such as the back. These techniques are well illustrated in both picture and verbal form. Normal findings and values are discussed as well as abnormal as they relate to various diseases and injuries, but with special emphasis on Rheumatology. There is no discussion regarding lab diagnosis or treatment of joint problems.

The authors have quoted Goethe to express the purpose of the publication—"What one knows, one sees." They have certainly done a commendable job in presenting information for this purpose.

HAROLD B. STRAUCH, M.D.

\* \* \*

**FRACTURE PROBLEMS—Problem Cases from Fracture Grand Rounds at the Massachusetts General Hospital**—William Hamilton Harris, M.D., Clinical Associate in Orthopedic Surgery, Harvard Medical School, Boston, Mass.; Assistant Orthopedic Surgeon, Massachusetts General Hospital, Boston, Mass.; Consultant in Orthopedic Surgery, United States Naval Hospital, Chelsea, Mass.; William Norman Jones, M.D., Instructor in Orthopedic Surgery, Harvard Medical School, Boston, Mass.; Assistant Orthopedic Surgeon, Massachusetts General Hospital, Boston, Mass.; and Otto E. Aufranc, M.D., Assistant Professor of Orthopedic Surgery, Harvard Medical School, Boston, Mass.; Chief of Fracture Clinic and Visiting Orthopedic Surgeon, Massachusetts General Hospital, Boston, Mass. The C. V. Mosby Company, St. Louis, Mo., 1965. 371 pages, \$20.00.

Much of the material in this book will be familiar to readers of the Journal of the American Medical Association, since the book is based upon the cases published as "Fracture of the Month," in the Journal, from July 1960, to July 1964. The book consists of 48 case studies of problem fractures. All anatomical segments of the skeletal system are covered, but by no means comprehensively. The clinical interpretations and management of the cases presented is by a distinguished group of orthopaedic surgeons, conducting a renowned fracture service. A consultant group referred to as guest participants includes well



known authorities. The concise discussions by the guest participants frequently were outstanding. Conflicting viewpoints were faithfully presented, giving testimony that "there are many roads to Rome." A high standard of practice was evident, and of course expected from such an able group of orthopaedic surgeons. In most instances the "cutting doctors" won out over the conservatives, and the method chosen usually led to the operating room and to the abundant supply of appliances for internal fixation. At a time when in many quarters the problem fractures of the tibia are less often treated by internal fixation and open reductions, the majority of the cases in this treatise were treated by open reduction, and in the diaphyseal fractures, more often than not, the transfixion was by a Lottes medullary rod.

Physical qualities of the book are good and the numerous roentgenograms are well reproduced.

The authors of this book would be the first to agree that the methods selected at MGH would not necessarily be the best, and certainly not the only good methods in other settings. It may be a matter for regret if certain of the methods presented are adopted in situations and settings where the method is not appropriate.

Textbook type of information is not presented, but the material presented would represent excellent supplementary reading and many pearls will be found by orthopaedic surgeons and others skilled in the management of problem fractures.

J. VERNON LUCK, M.D.

\* \* \*  
**PERSPECTIVES IN VIROLOGY IV**—Edited by Morris Pollard, Lobund Laboratory, University of Notre Dame, South Bend, Indiana. Harper & Row, Publishers (Hoeber Medical Division), New York, 1965. 317 pages, \$10.50.

This volume, the fourth in the series, is a record of a conference held in October 1964 in New York under the auspices of the Gustav Stern Foundation to discuss the most significant recent developments in virology. This particular conference was dedicated to a consideration of "hidden viruses"; i.e., agents which are not primarily cytotoxic and usually manifest phenomena of latency. A delightful introduction by T. Francis recounts personal and professional events in the life of Richard Shope to whom this conference was dedicated.

Subsequent chapters summarize studies on latent infections in insects, plants, and animals with particular emphasis on experimental models which may aid in the understanding of mechanisms of latency. Much emphasis is placed on "defective viruses," the genome of which is incomplete in some way; e.g., in the ability to direct synthesis of a protein coat. Such agents may require "helper" viruses such as seen among Rous sarcoma strains.

These and other topics of tumor virology are discussed in separate brief chapters followed by a record of the ensuing discussion. The formal contributions are written by outstanding investigators. Most of the presentations are clear and concise, but all of them are addressed to the professional virologist and contain much technical slang. A majority of presentations are summaries of material published elsewhere and thus do not present new results or concepts. Perhaps the greatest value of the volume lies in the accumulation of thoughts and results of leading investigators in tumor virology and related areas.

In the opinion of this reviewer, few physicians will be interested in this volume unless they work actively in virology. Libraries serving research centers will buy the volume—they buy all serial volumes—and thus will afford individuals the opportunity of perusing this compilation.

ERNEST JAWETZ, M.D., Ph.D.

**CURRENT CONCEPTS OF CLINICAL GASTROENTEROLOGY**—Edited by John R. Gamble, M.D., Clinical Instructor in Medicine, University of California School of Medicine; Chief, Gastroenterology Clinic, Presbyterian Medical Center, San Francisco; and Dwight L. Wilbur, M.D., Clinical Professor of Medicine, Stanford University School of Medicine, Stanford. Little, Brown and Company, Boston, Mass., 1965. 282 pages, \$11.00.

This book is composed of selected presentations given as part of a postgraduate course on "Progress in Gastroenterology" sponsored by the American Gastroenterological Association in cooperation with the University of California School of Medicine, San Francisco, in May, 1963. The participants in the course were all distinguished investigators and clinicians and the material they presented bears the mark of authority.

Among the subjects selected for reproduction in the book are the following: assessment of gastric secretion; hormonal factors influencing gastric secretion; the effect of serotonin and various hormones on the gastrointestinal tract; newer aspects of pancreatic disease; gastrointestinal responses in connective tissue disease; newer information regarding hepatic circulatory changes, the ultrastructure of the liver, bilirubin metabolism, and the role of the liver fat metabolism; and the deleterious effects of drugs on the gastrointestinal tract. The emphasis throughout is on summarization of current knowledge. Each presentation is concise and informative and the accompanying illustrative material and tabular data are well chosen and organized.

For those who wish a neatly-printed, compact book in which may be found succinct summaries of newer information on certain important aspects of the structure, function, and disorders of the gastrointestinal tract, this volume may be highly recommended.

J. EDWARD BERK, M.D.

\* \* \*  
**PROGRESS IN MEDICAL GENETICS—Volume IV**—Edited by Arthur G. Steinberg, Ph.D., Professor of Biology, Department of Biology, and Associate Professor of Human Genetics, Department of Preventive Medicine, Western Reserve University, Cleveland, Ohio; and Alexander G. Bearn, M.D., Professor, The Rockefeller University; Senior Physician, Hospital of the Rockefeller University, New York. Grune & Stratton, Inc., New York and London, 1965. 280 pages, \$12.75.

Progress in Medical Genetics is a well written, informative, collection of review articles on selected topics related to medical genetics. Although the editors have wisely chosen specific subjects of broad general interest, the book represents a compendium of detailed reviews rather than a comprehensive review of all developments in this rapidly progressing field. Each of the eight monographs has been written by researchers of distinction and, in general, each article is readily comprehensible by a physician with only a peripheral interest in the particular subject. The choice of topics reviews a wide subject range, and almost every reader will find one or more articles of particular interest to him. Most of the authors admirably link basic science knowledge with clinical manifestations and provide sufficient background information that both the basic science and clinical information are meaningful. Furthermore, the techniques employed in the various areas of research are described in sufficient detail to enable the reader to comprehend general principles without being overwhelmed with a maze of specific details. Chapters are well referenced, including many articles published within the last year. This book is to be highly recommended to any physician who maintains an interest in recent developments in the selected topics of medical genetics.

ALAN WINKELSTEIN, M.D.

# *application for* **HOTEL ACCOMMODATIONS**

## **NINETY-FIFTH *Annual Session***

**CALIFORNIA MEDICAL ASSOCIATION • MARCH 19-23, 1966**  
**BILTMORE HOTEL, LOS ANGELES**

House of Delegates Opening Session, Saturday evening, March 19; Special Conferences start March 19;  
 Scientific Assemblies start Sunday morning, March 20.

1. Fill in the form below **completely** for room accommodations at the CMA's 1966 Annual Session. There is only a limited number of rooms available. Your choice of accommodations will be better if your request is for rooms to be occupied by two or more persons.
2. Your reservation request should include the definite date and hour of your arrival and departure.
3. All reservations must be made through the CMA Housing Bureau, 693 Sutter Street, San Francisco, California 94102.
4. **DEADLINE** for housing: March 4, 1966.

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STATLER-HILTON			Suites
930 Wilshire Boulevard.....	10.00-17.50	16.00-22.50	30.00-65.00

\*Rates subject to change

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Please reserve the following accommodations for the CMA's 1966 Annual Session in Los Angeles, March 20-23, 1966. The first meeting of the House of Delegates begins Saturday evening, March 19; Scientific Programs begin March 20.

Single Bedroom \$.....Twin-Bedded Room \$.....Double Bedroom \$.....

Small Suite \$.....Large Suite \$.....Other \$.....

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 p.m. p.m.

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95th



*annual session*

P R O G R A M



Biltmore Hotel, Los Angeles

MARCH 19 to 23, 1966



Scientific Sessions • Technical Exhibits

Motion Picture Symposia

Closed-Circuit Television Symposia

Meetings of the House of Delegates



CALIFORNIA MEDICAL ASSOCIATION

# C.M.A. ANNUAL MEETING—1966

## SCIENTIFIC SESSIONS

LOCATION	Saturday, March 19	Sunday, March 20	Monday, March 21	Tuesday, March 22	Wednesday, March 23
<b>BILTMORE HOTEL</b>	A.M.	A.M.	A.M.	A.M.	A.M.
	P.M.	P.M.	P.M.	P.M.	P.M.
<b>Biltmore Bowl</b>	7:00 p.m. House of Delegates Opening Session			4:00 p.m. House of Delegates	9:00 a.m. House of Delegates
<b>Ballroom</b>		9:30 a.m. Problems of Office Management C.M.A.A.	9:30 a.m. Internal Medicine (Cardiology)	9:30 a.m. General Meeting Renal Failure	9:30 a.m. Internal Medicine (Gastroenterology)
		2:00 p.m. General Meeting Coronary Artery Disease	2:00 p.m. General Meeting Gastrointestinal Hemorrhage		
<b>Galeria Room</b>	9:00 a.m. to 4:30 p.m. Council of the C.M.A.	9:00 a.m. Pathology	9:30 a.m. General Practice Obstetrics Gynecology	9:00 a.m. Physicians' and School Administrators' Conference	9:30 a.m. General Practice Psychiatry and Neurology
		2:00 p.m. General Surgery	Noon Ob/Gyn Lunch	2:00 p.m.	2:00 p.m. Psychiatry and Neurology
<b>Renaissance Room</b>	9:30 a.m. Prevention Radiology Conference				
	1:30 p.m.				
<b>Ballroom Foyer</b>	9:00 a.m. Conference on Occupational Health		9:15 a.m. Rheumatic Diseases Conference		
	1:45 p.m.				
<b>Conference Room 1</b>	2:00 p.m. Infant Mortality Conference	9:00 a.m. Dermatology	9:00 a.m. General Surgery	9:30 a.m. Disaster Medical Care	2:00 p.m. Adverse Drug Reactions Conference
<b>Conference Room 2</b>	2:00 p.m. Cancer Conference Lump in the Neck	9:30 a.m. Radiology		10:30 a.m. Urology	
<b>Conference Room 4</b>	9:00 a.m. Pathology Conference and Section Business Meeting	9:00 a.m. Pediatrics	9:30 a.m. Environmental Health Conference		
	2:00 p.m.	12:30 p.m. Pediatrics Luncheon Meeting	1:30 p.m. Preventive Medicine		
<b>Conference Room 8</b>		9:30 a.m. Anesthesiology	9:30 a.m. Industrial Medicine and Surgery, and Physical Medicine		
		2:00 p.m. Allergy	2:00 p.m.		
<b>Conference Room 9</b>		9:30 a.m. Otolaryngology			
		2:00 p.m. Ophthalmology			
<b>Conference Room 10</b>		9:15 a.m. Orthopedics			
		2:30 p.m. Medicine & Relig.			
<b>Rendezvous Room</b>		9:00 a.m. Allergy			
		Film Symposium 9:00 a.m. Surgery	9:00 a.m. Radiation	9:00 a.m. Colonie Resection	Film Symposium 2:00 p.m. General Program
<b>Music Room</b>			9:00 a.m. Diabetes 10:30 a.m. Neurological Examination	2:00 p.m. CNS Infections	2:00 p.m. General Program

### SCIENTIFIC AND TECHNICAL EXHIBITS

#### Rex Room

9:00 a.m. to 5:00 p.m.  
Sunday through Tuesday

Wednesday: 9:00 a.m. to 3:00 p.m.



# Scientific Program

CALIFORNIA  
MEDICAL  
ASSOCIATION

*Ninety-Fifth  
Annual Session*

Biltmore Hotel

LOS ANGELES  
March 19 to 23\*†  
1966

\*House of Delegates  
Opening Meeting  
Saturday, March 19  
7:00 p.m.

†Special Conferences Start  
Saturday, March 19  
9:00 a.m.  
See pages 14 to 18

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# Information

**BADGES.** It is important that badges be worn at all times. Admission to scientific meetings is by badge only.

**COUNCIL.** The first meeting of the Council will be held in the Galeria Room, Friday, March 18 at 4:00 p.m., reconvening Saturday, March 19, 9:00 a.m. to 4:30 p.m., Galeria Room.

Further meetings will be held at 7:30 a.m. or 8:00 a.m., Sunday through Wednesday.

**DELEGATES.** For list of delegates, meeting times, places and agenda, see pages 44 to 49.

**EMERGENCY CALLS AND MESSAGES.** Convention Emergency Call Number: 213 629-6416—8:30 a.m. to 4:30 p.m., Saturday, March 19 through Wednesday, March 23.

**MESSAGE CENTER (213 629-6416)**—*Provided through the courtesy of the Pacific Telephone and Telegraph Company*—Registration Desk, Galeria—Open 8:30 a.m. to 4:30 p.m.—The Association will *attempt* to transmit messages to the individual physician. Each physician should notify his own office of the exact times and meetings he plans to attend, and the convention number.

**TECHNICAL EXHIBITS**—Rex Room. See pages 67 to 74.

**SCIENTIFIC EXHIBITS**—Rex Room. See page 41.

**ORGANIZATIONAL EXHIBITS**—South Galeria. See page 41.

**MOTION PICTURE SYMPOSIA** will be shown in the Music Room. See program synopsis, page 40.

**TELEVISION SYMPOSIA** will be shown in the Music Room. See program synopsis, page 40.

*You are urged to visit and attend all exhibits.*

**MEETING TIMES AND PLACES.** See chart on page 2 for exact times and places of general and section meetings.

**REGISTRATION.** Registration and information desks are located in the Galeria. *All members, guests, and visitors are requested to register immediately on arrival.* There is no charge for registration. Registration desks are open Saturday through Wednesday. *Admission to the general and section sessions and exhibit area is by badge only.*

Members wishing to vote in specialty sections must indicate appropriate section when registering; voting in other sections will not be allowed.

**QUALIFICATIONS/REQUIREMENTS FOR REGISTRATION.** (a) All M.D.'s with credentials showing that they hold valid license to practice medicine. (Membership card in C.M.A.; county medical society/association or A.M.A. membership card.) (b) Medical students will be admitted upon presentation of credentials from their medical schools identifying them as medical students. (A membership card of the Student American Medical Association or letter from their dean's office.) (c) Medical assistants will be admitted upon presentation of a letter from the physician-employer or C.M.A.A. membership card. (d) Military paramedical personnel will be admitted upon presentation of a letter requesting their admittance, written by their commanding officer. (e) Dentists (D.D.S.), doctors of veterinary medicine (D.V.M.), registered nurses (R.N.), student nurses, x-ray technicians, laboratory technicians, allied public health personnel, and others will be admitted provided they have proper identification. (f) *All questions on admission will be passed upon by a member of the Committee on Registration who will be present at the desk.*



#### ■ FRIDAY, MARCH 18

Medical Executives Conference—Conference Room 8, 12:00 p.m. to 5:00 p.m.

#### ■ SATURDAY, MARCH 19

CMA HOUSE OF DELEGATES OPENING SESSION—Biltmore Bowl, 7:00 p.m.

CALPAC Meeting—Biltmore Bowl, immediately following the Opening Session of the CMA House of Delegates.

American College of Chest Physicians—Conference Room 10, 8:00 a.m. to 5:00 p.m.

California Federation of Pediatric Societies Meeting—Conference Room 9, 1:30 p.m. to 5:00 p.m.

California Society of Anesthesiologists—Conference Room 8, 8:00 a.m. to 5:00 p.m.

California Physicians' Service Board Meeting—Conference Room 5, 4:00 p.m.; Dinner—Conference Room 4, 6:00 p.m.

Conference on Occupational Health Luncheon—Ballroom, 12:00 noon.

Los Angeles and Metropolitan Dermatological Societies—Good Hope Clinic, 1241 Shatto, Los Angeles, 2:30 p.m.

Reference Committee Chairmen Luncheon and Meeting—Conference Room 5, 12:00 noon.

#### ■ SUNDAY, MARCH 20

CMA PRESIDENTS' RECEPTION honoring the Presidents of the California Medical Association and the Woman's Auxiliary, Renaissance Room, 6:30 p.m.

CMA Section on Allergy Luncheon—Rendezvous Room, 12:00 noon.

CMA Section on Pediatrics Luncheon with the Council of Pediatric Societies—Conference Room 4, 12:30 p.m.

#### ■ MONDAY, MARCH 21

AMA Delegates Meeting—Conference Room 5, 2:00 p.m.

Bureau of Medical Economics Meeting and Luncheon—Conference Room 3, 9:00 a.m. to 5:00 p.m.

CMA Section on Obstetrics and Gynecology Joint Luncheon Meeting with the California Division of the American College of Obstetricians and Gynecologists—Galeria Room, 12:00 noon.

Yale Alumni Reception—Conference Room 1, 5:30 p.m.

#### ■ TUESDAY, MARCH 22

CMA Past Presidents' Luncheon—Conference Room No. 9, 12:00 noon.

California Medicine-Editorial Board Luncheon—Conference Room 10, 12:15 p.m.

Conference on Disaster Medical Care Luncheon—Conference Room 5, 12:00 noon.

Conference of Physicians and School Administrators Luncheon—Renaissance Room, 11:45 a.m.

Medical Friends of Wine Reception—Galeria Room, 7:00 p.m.

Stanford Alumni Breakfast—Conference Room 4, 7:30 a.m. to 9:00 a.m.

#### ■ WEDNESDAY, MARCH 23

California Physicians' Service Lunch and Meeting—Conference Room 4, 12:00 noon to 5:00 p.m.

## *Other Meetings and Entertainment*

CALIFORNIA  
MEDICAL  
ASSOCIATION

RALPH C.

*Teall*

*president*



JAMES C.

*MacLaggan*

*president-elect*





# *Guest Speakers*



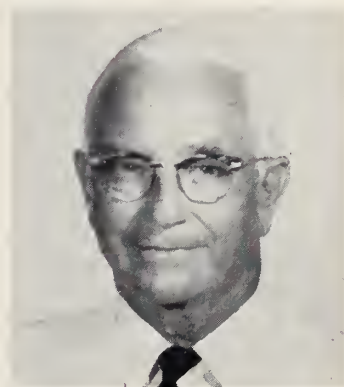
CHARLES K. FRIEDBERG



BERNARD LOWN



BELDING H. SCRIBNER



OWEN H. WANGENSTEEN

■ CHARLES K. FRIEDBERG, M.D., Associate Clinical Professor of Medicine, Columbia University School of Medicine, New York, New York

■ BERNARD LOWN, M.D., Assistant Professor of Medicine, Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts

■ BELDING H. SCRIBNER, M.D., Professor of Medicine, University of Washington School of Medicine, Seattle, Washington

■ OWEN H. WANGENSTEEN, M.D., Professor and Chairman, Department of Surgery, University of Minnesota, Minneapolis, Minnesota

# *Out-of-State Guests of Sections and Organizations*

## *Allergy—*

- REXFORD G. HAYCRAFT, Major, M.C., United States Air Force, Offutt Nebraska

## *Anesthesiology—*

- PHILIP R. BROMAGE, M.D., Montreal, Quebec, Assistant Professor, Department of Anesthesiology, McGill University School of Medicine
- MAX SAMTER, M.D., Chicago, Illinois, Professor of Medicine, University of Illinois Medical Center
- GORDON L. SNIDER, M.D., Chicago, Illinois, Chief, Division of Thoracic Medicine, Mt. Sinai Hospital

## *General Surgery—*

- J. A. MONCRIEF, Colonel, M.C., United States Army, San Antonio, Texas, Commander and Director United States Army Surgical Research Unit, Brooke Army Medical Center

## *Obstetrics and Gynecology—*

- RONALD J. PION, M.D., Seattle, Washington, Assistant Professor of Obstetrics and Gynecology, University of Washington School of Medicine

## *Ophthalmology—*

- ALSTON CALLAHAN, M.D., Birmingham, Alabama
- DAN M. GORDON, M.D., New York, New York, Professor of Ophthalmology, Cornell University Medical College

## *Pathology—*

- DANIEL M. BAER, M.D., Portland, Oregon, Pathologist, Providence Hospital Laboratory

## *Pediatrics—*

- E. H. CHRISTOPHERSON, M.D., Evanston, Illinois, Executive Director, American Academy of Pediatrics

## *Preventive Medicine and Public Health—*

- J. GORDON BARROW, M.D., Atlanta, Georgia, Director, Cardiovascular Control Services, State of Georgia Department of Health

## *California Student Health Study—Committee on School Health—*

- FRED V. HEIN, Ph.D., Chicago, Illinois, Director of Department of Health Education, American Medical Association
- JULIUS RICHMOND, M.D., Washington, D.C., Director, Head Start Program, Office of Economic Opportunity

## *Committee on Dangerous Drugs and Adverse Reactions—Conference on Adverse Drugs—*

- JOHN J. MERENDINO, M.D., Washington, D.C., Deputy Director, Food and Drug Administration, Department of Health, Education, and Welfare

## *Conference on Cancer—Los Angeles Branch of the American Cancer Society*

- EDGAR L. FRAZELL, M.D., New York, New York, Chief, Head and Neck Service, Memorial Hospital for Cancer and Allied Diseases

## *Conference on Environmental Health—Committee on Environmental Health—*

- MALCOLM HARGRAVES, M.D., Rochester, Minnesota, Senior Consultant, Mayo Clinic

## *Conference on Occupational Health—Committee on Occupational Health & Rehabilitation*

- ALEXANDER HIRSCHFELD, M.D., Detroit, Michigan
- D. JOHN LAUER, M.D., New York, New York, Medical Director, International Telephone and Telegraph Corporation

## *Northern California Rheumatism Association and Southern California Rheumatism Society—*

- MORRIS ZIFF, M.D., Dallas, Texas, Professor of Internal Medicine, University of Texas School of Medicine

## *Interagency Cancer Conference—*

- SIDNEY J. CUTLER, Sc.D., Bethesda, Maryland, Head of End Result Section, Clinical Biometry Branch, National Cancer Institute



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# Scientific Sessions

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## ■ GENERAL MEETINGS

### FIRST GENERAL MEETING

SUNDAY, MARCH 20

2:00 p.m.—Ballroom, Galeria Floor

### Coronary Artery Disease

#### 2:00— Symposium on General Care in Coronary Artery Disease

Moderator: John J. Sampson, M.D., San Francisco

2:00—Coronary Care Units (Myocardial Infarction)—  
Bernard Lown, M.D., Boston, by invitation.

2:15—Care of Shock and Heart Failure in Acute Myo-  
cardial Infarction—Eliot Corday, M.D., Los An-  
geles.

2:35—Physical Activity During and Following Acute  
Myocardial Infarction—Robert Stivelman, M.D.,  
Los Angeles.

2:50—General and Psychological Care of the Patient with  
Acute Myocardial Infarction—Charles K. Fried-  
berg, M.D., New York, by invitation.

3:15—Recess.

#### 3:30— Symposium on Arrhythmias

Moderator: George C. Griffith, M.D., Los Angeles

3:30—Value of Monitoring for Arrhythmias—Herman N.  
Uhley, M.D., San Francisco.

3:45—Management of Ectopic Arrhythmias — Bernard  
Lown, M.D., Boston, by invitation.

4:05—Third-degree Heart Block—Charles K. Friedberg,  
M.D., New York, by invitation.

4:30—Mechanisms of Drug Therapy in Arrhythmias and  
Dynamic Defects—Albert A. Kattus, Jr., M.D., Los  
Angeles.

5:00-6:00—Small Group Discussions.



## **Gastrointestinal Hemorrhage**

2:00—

### **Panel Discussion**

#### **Major Gastrointestinal Hemorrhage**

Moderator: Clarence J. Berne, M.D., Los Angeles

Members of the Panel: Owen H. Wangensteen, M.D., Minnesota, by invitation; Parker R. Beamer, M.D., Los Angeles, by invitation; J. Edward Berk, M.D., Harvey I. Meyers, M.D., and W. Russell Smith, M.D., all from Los Angeles.

This session will be a discussion and an analysis of case presentations prepared by Doctor Clarence J. Berne and the panelists. Several microphones will be placed in the audience to encourage the questions and discussions that make for a lively program.

## **Therapy of Uremia**

Moderator: Morton H. Maxwell, M.D., Los Angeles

9:30—**The Uremic Syndrome**—Harvey C. Gonick, M.D., Los Angeles.

9:45—**Fluid and Electrolyte Disturbances of Uremia**—Paul F. Gulyassy, M.D., San Francisco, by invitation.

10:15—**The Work-Up of the Uremic Patient**—Arthur Gordon, M.D., Los Angeles.

10:35—**Conservative Treatment of Acute Renal Failure**—Telfer B. Reynolds, M.D., Los Angeles.

10:55—**Conservative Treatment of Chronic Uremia**—Charles R. Kleeman, M.D., Los Angeles.

11:15—**Role of Dialysis in Uremia**—Belding H. Scribner, M.D., Seattle, by invitation.

11:35—**Surgery and Uremia**—Stanley S. Franklin, M.D., Los Angeles.

11:55—

### **Panel Discussion**

#### **Treatment of Uremia: Conservative, Dialysis, Transplantation**

Moderator: Milton Rubini, M.D., Los Angeles, by invitation

Members of the Panel: Belding H. Scribner, M.D., Seattle, by invitation; Paul F. Gulyassy, M.D., San Francisco, by invitation; Arthur Gordon, M.D., and Telfer B. Reynolds, M.D., Los Angeles.

## **SECOND GENERAL MEETING**

**MONDAY, MARCH 21**

**2:00 p.m.—Ballroom, Galeria Floor**

## **THIRD GENERAL MEETING**

**TUESDAY, MARCH 22**

**9:30 a.m.—Ballroom, Galeria Floor**

# PRE-CONVENTION & CONVENTION

## *special conferences*

**SATURDAY, MARCH 19—9:30 a.m. to 3:30 p.m.—Renaissance Room, Galeria Floor**

### **RADIOLOGY CONFERENCE**

**Committee on Cancer, California Medical Association**

*Chairman:* Stanley A. Moore, M.D., San Diego • *Secretary:* John F. Weigen, M.D., Palo Alto

#### **THERAPY SESSION—9:30 a.m. to 11:30 a.m.**

Departing from prior case presentation format, a panel discussion of three common therapeutic problems will be held, with audience participation encouraged.

#### **DIAGNOSTIC SESSION—1:30 p.m. to 3:30 p.m.**

Diagnostic cases with histories and films will be presented. Cases have been selected to illustrate specific problems in the radiological and clinical diagnosis of cancer. Audience participation and discussion are urgently requested.

### **SATURDAY, MARCH 19—9:00 a.m.—Ballroom Foyer, Galeria Floor**

#### **CONFERENCE ON OCCUPATIONAL HEALTH INJURY AND DISEASE—ITS EMOTIONAL IMPACT**

##### **9:00—Registration**

Presiding: Edward J. Zaik, M.D.

CMA Committee on Occupational Health  
and Rehabilitation, Los Angeles

##### **9:30—Welcome—Ralph C. Teall, M.D., President, California Medical Association**

**Purpose of the Conference—**Carl E. Anderson,  
M.D., Chairman of the Council, California  
Medical Association

##### **9:40—Symposium**

**Education Needs—Are They Special?**

Moderator: Jean S. Felton, M.D., Professor of  
Occupational Health, U.C. Center for the  
Health Sciences, Los Angeles, by invitation

1. **In Safety Programs—**Walter Stikeleather,  
Plant Safety Supervisor, Pacific Telephone  
Co., Los Angeles, by invitation

2. **For Physicians and Nurses—**D. John Lauer,  
M.D., Medical Director, International Tele-  
phone and Telegraph Corporation, New  
York, N.Y., by invitation

3. **For Claims Personnel and Industrial Rela-  
tions—**Howard D. Craighton, Plant Per-  
sonnel Supervisor, Pacific Telephone Co.,  
Los Angeles, by invitation

##### **10:30—Questions and Answers**

##### **10:45—Recess**

- 11:00—**The Detroit Pilot Program—**Alexander  
Hirschfeld, M.D., Detroit, Michigan, by invi-  
tation

##### **12:00—Luncheon—Ballroom, Galeria Floor**

Presiding: Packard Thurber, Jr., M.D.,  
Chairman, CMA Committee on  
Occupational Health and Rehabilitation

**Compensable Injuries—**Alexander Hirschfeld,  
M.D., Detroit, Michigan, by invitation

### **SATURDAY, MARCH 19—1:45 p.m.—Galeria Room, Galeria Floor**

- 1:45—**The Emotional Impact: Patient Interview—  
Video Tape Presentation—**Allen J. Enelow,  
M.D., Los Angeles

##### **2:15—Panel Discussion**

Moderator: Allen J. Enelow, M.D.,  
Postgraduate Psychiatry Department,  
University of Southern California, Los Angeles

**Members of the Panel:**

1. Alexander Hirschfeld, M.D., Detroit, Mich-  
igan, by invitation
2. Industrial Physician — Robert Anderson,

M.D., Division of Industrial Accidents, Pa-  
cific Telephone Co., San Francisco

3. **Industrial Relations—**Milton Holmen, Per-  
sonnel Manager, Systems Development  
Corporation, Santa Monica, by invitation
4. **Labor—**Charles Scully, Legal Counsel, Cal-  
ifornia AFL-CIO, San Francisco, by invi-  
tation
5. **Division of Industrial Accidents—**Thomas  
N. Saunders, Administrative Director, Di-  
vision of Industrial Accidents, San Fran-  
cisco, by invitation

- 4:30—**Concluding Statements—**Packard Thurber,  
Jr., M.D., Los Angeles



**SATURDAY, MARCH 19—2:00 p.m.—Conference Room 4, Conference Room Floor**

**SYMPOSIUM ON CANCER**

**THE UBIQUITOUS LUMP IN THE NECK**

Presented by The American Cancer Society,  
Los Angeles Branch

Moderator: Edgar L. Frazell, M.D., New York City,  
by invitation

Members of the Panel: Robert J. Schweitzer, M.D.,  
Oakland, Robert S. Pollack, M.D., San Francisco,  
Emory S. Moore, M.D., Long Beach, Harvey P.  
Groesbeck, Jr., M.D., San Diego, Lewis W. Guiss,  
M.D., Los Angeles, and James T. Helsper, M.D.,  
Pasadena

Doctor Edgar L. Frazell, Chief of the Head and Neck  
Service at the Memorial Hospital for Cancer and  
Allied Diseases, will discuss first the primary  
problem of the patient who presents with a sus-  
picious neck nodule. The members of the panel  
will then present their experiences related to  
primary tumors of the head and neck, which me-  
tastasize to the neck, and their management of  
such problems. The presenting complaint, rather  
than symptoms referable to the primary tumor,  
will be given. Doctor Frazell will comment upon  
each presentation, comparing it with the pro-  
cedures and results of Memorial Hospital

**SATURDAY, MARCH 19—2:00 p.m.—Conference Room 1, Conference Room Floor**

**CONFERENCE ON THE  
HEMOLYTIC DISEASE OF THE NEWBORN**

*Sponsored by the Committee on Maternal and Child Care,  
California Medical Association, and the California State  
Department of Public Health*

**2:00— Round Table Discussion**

**Hemolytic Disease of the Newborn:  
Present and Future Methods of Prevention  
and Treatment**

Moderator: Talcott Bates, M.D., Monterey

Participants: Carol B. Hyman, M.D., Los An-

geles, Joseph H. Kushner, M.D., Jimmie A.  
Westberg, M.D., both San Francisco, and  
Arthur J. Rollins, M.D., Willows

The Committee on Maternal and Child Care  
and the California State Department of  
Public Health completed in 1965 a three-  
year study of all hemolytic deaths in new-  
born infants. This Conference will be of  
interest and importance to general practi-  
tioners, obstetricians, pediatricians and  
other physicians responsible for infant  
care. The program will emphasize practi-  
cal preventive and treatment methods

**SUNDAY, MARCH 20—9:30 a.m.—Ballroom, Galeria Floor**

**SPECIAL CONFERENCE ON PROBLEMS OF  
OFFICE MANAGEMENT**

*Sponsored by the California Medical  
Assistants Association*

General Chairman: Erna de Nu, Hayward

**9:30— Panel Discussion**

**"Doctor, What You Don't Know Can Hurt You"**

Moderator: Charlotte C. Baer, M.D., San Francisco

Members of the Panel: Robert D. Huber,  
LL.B., San Francisco, Henry Bodner, M.D.,  
Van Nuys, Mary Kinn, Santa Ana, Erna de  
Nu, Hayward, and Dorothy Hyde, Fresno

There will be a visual demonstration of sev-  
eral important mistakes with a critique  
and discussion by the panel of ways to  
prevent or correct these mistakes

The purpose of this program is to assist phy-  
sicians in improving office management pro-  
cedures

**SUNDAY, MARCH 20—2:30 p.m.—Rendezvous Room, Galeria Floor**

**FIRST CONFERENCE ON MEDICINE AND  
RELIGION**

*Sponsored by the CMA Committee on Medicine and  
Religion*

Chairman: Roger W. Barnes, M.D., Los Angeles  
of CMA Committee on Medicine and Religion

**2:30—Welcome—Roger W. Barnes, M.D., Chairman**

**2:40— Teamwork**

**The Physician, the Clergyman, and the Patient with  
Terminal Illness**

Moderator: The Reverend Dr. Paul B. McCleave,  
Director of AMA Department of Medicine  
and Religion, by invitation

**2:40—Introduction—The Reverend Dr. Paul B. Mc-  
Cleave, Chicago, by invitation**

**2:55—The Clergyman's Viewpoint—Bishop Tim-  
othy Manning, Vicar General, Archdiocese of  
Los Angeles, by invitation**

**3:20—The Physician's Viewpoint—Albert E. Long,  
M.D., San Francisco**

**3:45—Panel Discussion—Questions from the Audi-  
ence**

**4:00—Medicine and Religion in Component Societies  
—Ronald D. Smith, M.D., Fresno**

**MONDAY, MARCH 21—9:15 a.m.—Ballroom Foyer, Galeria Floor**

**CONFERENCE ON RHEUMATIC DISEASES**

*Sponsored by the Northern California Rheumatism Association, the Southern California Rheumatism Society, and the Arthritis Foundation, Northern and Southern California Chapters*

Presiding: Martin A. Shearn, M.D., El Cerrito

- 9:15—**Laboratory Aids in the Diagnosis of Rheumatic Diseases**—Morris Ziff, M.D., Dallas, Texas, by invitation
- 10:00—**The Surgical Treatment of Arthritis**—Leonard Marmor, M.D., Los Angeles

10:45—Recess

11:00— **Panel Discussion**

Presiding: Melvin R. Kaplan, M.D., San Gabriel

**Treatment of Rheumatoid Arthritis**

Moderator: Ephraim P. Engleman, M.D., San Mateo

Members of the Panel: Joseph E. Giansiracusa, M.D., San Jose; Virgil Hanson, M.D., Los Angeles; J. Paul Harvey, Jr., M.D., Los Angeles; William R. Murray, M.D., San Francisco

**MONDAY, MARCH 21—9:30 a.m.—Conference Room 4, Conference Room Floor**

**CONFERENCE ON ENVIRONMENTAL HEALTH**

Chairman: Francis M. Pottenger, Jr., M.D., Monrovia

9:30— **Panel Discussion**

**Diagnosis and Treatment  
of Pesticide Induced Illnesses**

Moderator Irma C. West, M.D., Berkeley

Members of the Panel: Rutherford T. Johnstone, M.D., Los Angeles, and Malcolm Hargraves, M.D., Rochester, Minn., by invitation

1. **Public Health Aspects**—Irma C. West, M.D., Berkeley
2. **Toxicology and Diagnosis**—Rutherford T. Johnstone, M.D., Los Angeles
3. **Treatment**—Malcolm Hargraves, M.D., Rochester, Minn., by invitation

10:55—**Occupational Health in Aerospace and Ground Support**—Dwight B. Culver, M.D., Azusa

11:35—**Dangers and Control of Water Borne Diseases in California**—Frank M. Stead, Berkeley, by invitation

**TUESDAY, MARCH 22—9:00 a.m.—Galeria Room, Galeria Floor**

**JOINT CONFERENCE FOR PHYSICIANS AND  
SCHOOL ADMINISTRATORS**

*Program Co-sponsored by the Committee on School Health, California Medical Association, California Association of School Administrators and the California Joint Study of Student Health Problems and School Performance*

General Chairmen: Gerald G. Jampolsky, M.D., Tiburon; B. Otis Cobb, M.D., Walnut Creek

9:00—**Addresses of Welcome**—James C. MacLaggan, M.D., President-Elect, California Medical Association, San Diego; Norman Sharer, Ph.D., Superintendent, Santa Barbara City Schools, Santa Barbara, by invitation

9:30— **Symposium**

**Health Needs of School Children—Should  
Physicians and School Administrators  
Fight or Switch?**

Presiding: Gerald G. Jampolsky, M.D., Tiburon

9:30—**Impact of Federal Programs on the Health of School Children**—Julius Richmond, M.D., Director, Head Start Program, Office of Economic Opportunity, Washington, D.C., by invitation

10:00—Recess

10:15—**Local Levels—Should School Administrators and Physicians Fight or Switch?**

1. **Problems and Specific Programs—School Administrators' Perception**—Louise Seyler, Ed.D., Deputy Superintendent, Los Angeles City Unified School District, Los Angeles, by invitation
2. **Problems and Specific Programs—Physicians' Perception**—Tom W. Robinson, M.D., Newport Beach

11:00— **Panel Discussion**

**Molehills to Mountains—Putting Local  
Problems Into Perspective**

Moderator: Richard Foster, Ed.D., by invitation

Members of the Panel: Glenn Austin, M.D., Los Altos; Clifford Thyburg, Covina, by invitation, Louise Seyler, Ed.D., Los Angeles, by invitation, and Tom W. Robinson, M.D., Newport Beach

11:45—**No-host Luncheon** (Preparation of questions for afternoon "Town Hall Meeting" panelists)—Renaissance Room, Galeria Floor



**TUESDAY, MARCH 22—2:00 p.m.—Galeria Room, Galeria Floor**

**CALIFORNIA JOINT STUDY OF STUDENT  
HEALTH PROBLEMS AND  
SCHOOL PERFORMANCE**

Presiding: Norman Sharer, Ph.D., Santa Barbara,  
by invitation

- 2:00—1. **Introduction and Objectives**—B. Otis Cobb,  
M.D., Walnut Creek  
2. **Funding the Study\***—Robert Osborn,  
D.V.M., Los Angeles, by invitation  
2:15—**Documentary Film**—Leonard J. Dolton, Ed.D.,  
Walnut Creek, by invitation  
2:45—**Health and Student Performance—Some Spe-  
cific Relationships**—B. Otis Cobb, M.D., Wal-  
nut Creek  
3:05—**Physician Respondent**—Maxine M. Sehring,  
M.D., Walnut Creek

\*The study was made possible by a grant from the Cali-  
fornia Dairy Council.

3:15—**Educator Respondent**—Harold Schoenfeld,  
Union City, by invitation

**3:30— Town Hall Panel Discussion**

**The Big Compromise**

Moderator: Byron H. Demorest, M.D., Sacramento

Members of the Panel: Thomas Braden,  
Oceanside; Keith Walton, Ed.D., Santa Fe  
Springs; Wilson Riles, Sacramento; Paul  
Hillar, Ed.D., Modesto, and Fred V. Hein,  
Ph.D., Chicago, all by invitation

(Questions from the audience are invited)

**4:45—Conclusion—**

1. Norman Sharer, Ph.D., Santa Barbara, by  
invitation
2. Ruth A. Frary, M.D., Watsonville

**TUESDAY, MARCH 22—9:30 a.m.—Conference Room 1, Conference Room Floor**

**DISASTER MEDICAL CARE**

**Theme: The Community in Action**

General Chairman: Donald E. Barker, M.D.,  
Van Nuys

9:30—**Welcome**—Wayne P. Chesbro, M.D., Berkeley

**9:35— Panel Discussion**

**Local Projects in Disaster Preparedness**

Moderator: Donald E. Barker, M.D., Van Nuys

9:35—**Planning Local Exercises**—Charles Hender-  
son, M.D., San Mateo

9:55—**Teaching the Allied Health Services**—Emile  
Meine, M.D., Panorama City

10:15—**Discussion**

**10:35— Panel Discussion**

**The Effects of the Watts Riot on Disaster  
Medical Care in Los Angeles**

Moderator: Frank F. Schade, M.D., Los Angeles

Members of the Panel: Milford X. Anderson,  
M.D., Los Angeles, and Kenneth H. Suther-  
land, M.D., Los Angeles

1. **"Disaster Strikes"**—Motion Picture—Los  
Angeles Fire Department
2. **The City in Action**—Milford X. Anderson,  
M.D., Los Angeles
3. **County Medical Care**—Kenneth H. Suther-  
land, M.D., Los Angeles
4. **Management of a Spreading Medical Prob-  
lem**—Frank F. Schade, M.D., Los Angeles  
Discussion

**TUESDAY, MARCH 22—2:00 p.m.—Conference Room 1, Conference Room Floor**

**INTERAGENCY CONFERENCE ON  
CANCER DIAGNOSIS, TREATMENT AND  
CONTROL IN CALIFORNIA**

Moderator: Lewis Guiss, M.D., Los Angeles

2:00—**Earlier Diagnosis of Cervical Cancer: An  
Analysis of Reports to the California Tumor  
Registry from 1942 to 1961**—George Linden,  
M.P.H., and John Dunn, M.D., Berkeley, both  
by invitation

2:30—**The Value of Mammography in Asympto-**

**matic Women**—G. Melvin Stevens, M.D., Palo  
Alto

3:00—**Prognostic Factors in Breast Cancer: The  
Value of Central Registry Data**—Sidney Cut-  
ler, Sc.D., Bethesda, Md., by invitation

3:45—**The Controversy Over Simple and Radical  
Mastectomy for Cancer of the Breast**—John  
W. Cline, M.D., San Francisco

4:15—**The Problems of Making Motion Pictures for  
Physicians on Leukemia and Gastric Cancer**  
—Sol R. Baker, M.D., Beverly Hills

**WEDNESDAY, MARCH 23—2:00 p.m.—Conference Room 1, Conference Room Floor**

**CONFERENCE ON ADVERSE DRUG REACTIONS**

*Co-sponsored by the Committee on Dangerous Drugs and Adverse Reactions, California Medical Association, and the California State Department of Public Health*

Moderator: John F. Murray, M.D., Fresno

2:00—A Joint Study of Deaths from Aplastic Anemia in California from January 1, 1963 to June 30, 1964—

A. Introduction—John F. Murray, M.D., Fresno

B. Preliminary Results—Ralph O. Waller-

stein, M.D., San Francisco, and John W. Brown, M.D., Berkeley

2:40—Marijuana—The Arguments For and Against Legal Control of Use—Edward R. Bloomquist, M.D., Glendale

Discussants—to be announced

3:40—Adverse Drug Experience Reporting System of the Food and Drug Administration—John J. Merendino, M.D., Washington, D.C., by invitation

Discussion

4:30—Summary—John F. Murray, M.D., Fresno

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**ACKNOWLEDGMENT**

A major objective of the Scientific Board in recent years has been the improvement of the Annual Scientific Assembly. The progress towards the attainment of this objective has been made possible by the work of many physicians, and the support of sections, committees, specialty societies and voluntary health agencies. Lack of space prevents the listing of these people and groups, but the California Medical Association is extremely appreciative of their cooperation.

Committee on Scientific Assemblies  
of the Scientific Board

VICTOR RICHARDS, M.D., *Chairman*



## INTERNAL MEDICINE

Chairman.....WALTER P. MARTIN, M.D., Long Beach  
 Secretary.....ROBERT L. PAVER, M.D., San Francisco  
 Assistant Secretary...JOHN L. BENTON, JR., M.D., Los Angeles

**MONDAY, MARCH 21**                      **9:30 a.m.—Ballroom  
 Galeria Floor**

*Program Co-sponsored by the American College of Cardiology*

Moderators: Robert W. Oblath, M.D., Sherman Oaks, and  
 Harold H. Rosenblum, M.D., San Francisco

9:30—Current Advances in the Treatment of Hyperten-  
 sion—William M. Smith, M.D., San Francisco, by  
 invitation

9:55—The Proper Use of Anticoagulants—Maxwell J.  
 Binder, M.D., Los Angeles

10:20—Recess

10:35—The Proper Use of Digitalis—Willard J. Zinn, M.D.,  
 Los Angeles

11:00—Trends in Evaluation and Management of Coronary  
 Artery Disease—Hyman W. Paley, M.D., San  
 Francisco

11:30—Considerations in the Treatment of Arrhythmias—  
 Bernard Lown, M.D., Boston, by invitation

**WEDNESDAY, MARCH 23**                      **9:30 a.m.—Ballroom  
 Galeria Floor**

9:30—                      **Symposium**

**Current Concepts in Therapy—  
 Gastrointestinal Disease**

Moderator: Walter P. Martin, M.D., Long Beach

9:30—Treatment of Neoplasia of the Gastrointestinal  
 Tract—Jesse L. Steinfeld, M.D., Los Angeles

9:55—Treatment of Pancreatitis and Its Complications—  
 Bernard J. Haverback, M.D., Los Angeles

10:20—Recess

10:30—Treatment of Chronic Hepatitis—Telfer B. Rey-  
 nolds, M.D., Los Angeles

10:55—Malabsorption State—Arthur D. Schwabe, M.D.,  
 Torrance

11:20—                      **Panel Discussion**

**Current Concepts in Therapy of Ascites**

Moderator: Walter P. Martin, M.D., Long Beach

Members of the Panel: Telfer B. Reynolds, M.D., Charles  
 R. Kleeman, M.D., William H. Bachrach, M.D., Ber-  
 nard J. Haverback, M.D., Los Angeles, and Arthur  
 D. Schwabe, M.D., Torrance

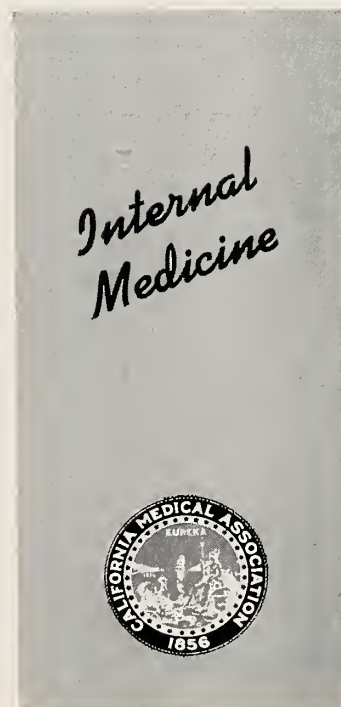
11:55—Business Meeting



WALTER P. MARTIN  
*Chairman*



ROBERT L. PAVER  
*Secretary*

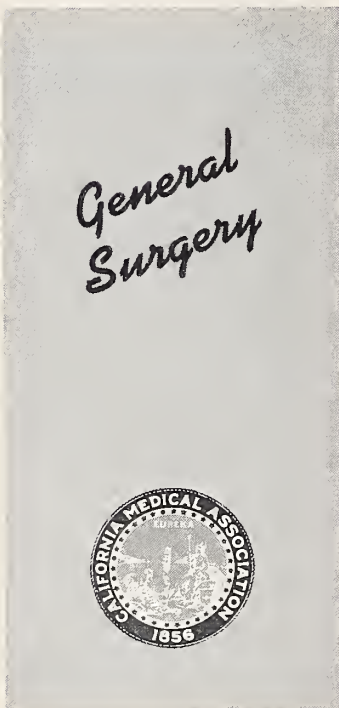




NEWLIN HASTINGS  
Chairman



ALBERT G. CLARK  
Secretary



## GENERAL SURGERY

Chairman.....NEWLIN HASTINGS, M.D., Los Angeles  
Secretary.....ALBERT G. CLARK, M.D., San Francisco  
Assistant Secretary...DAVID B. SHELDON, M.D., Pacific Palisades

SUNDAY, MARCH 20

2:00 p.m.—Galeria Room  
Galeria Floor

2:00—Experimental Air Embolism—Charles C. Wycoff,  
M.D., San Francisco

2:20— **Panel Discussion**

### Panel Discussion on Burns

Moderator: William H. Snyder, Jr., M.D., Los Angeles

Members of the Panel: Albert G. Clark, M.D., San Francisco, Sanford R. Dietrich, M.D., Santa Barbara, J. A. Moncrief, Colonel, M.C., U.S.A., San Antonio, by invitation, and John H. Winkley, M.D., Los Angeles

3:50—Recess

4:00—Postoperative Care of Mastectomy Patient—Clinton Ervin, Jr., M.D., San Mateo

4:20—Spectrum of Lung Cancer in Vivo and in Vitro—Russell P. Sherwin, M.D., Los Angeles, by invitation

4:40—Physiology and Metabolic Effect of Low Molecular Dextran in Oligemic Shock—William Schumer, M.D., Sacramento, by invitation

MONDAY, MARCH 21

9:00 a.m.—Conference Room 1  
Conference Room Floor

9:00—Total Colectomy and Ileoproctostomy With the Preservation of the Ileocecal Valve—Lawrence Braslow, M.D., Riverside

9:20— **Panel Discussion**

### Bowel Obstruction

Moderator: William P. Longmire, Jr., M.D., Los Angeles

Members of the Panel: Leo G. Rigler, M.D., Los Angeles, William Silen, M.D., San Francisco and Owen Wangersteen, M.D., Minneapolis, by invitation

10:50—Recess

11:00—Unsuspected Cancer Found During Minor Anorectal Surgery—Lewis I. Grodsky, M.D., San Francisco

11:20—Percutaneous Cholangiography in the Jaundiced Patient—Marvin James, M.D., La Mesa

11:40—Chairman's Address: The Medical Student—Newlin Hastings, M.D., Los Angeles

11:55—Business Meeting



*Chairman*.....LELAND B. BLANCHARD, M.D., San Jose  
*Secretary*.....J. BLAIR PACE, M.D., Oceanside  
*Assistant Secretary*...ALFRED F. KANDBINDER, M.D., Monterey

*Joint Meeting with Section on Obstetrics and Gynecology*  
**Advances in Therapy—Obstetrics and Gynecology**

10:00—**The Cul-de-sac Mass: A Pelvic Dilemma**—Prentiss Willson, M.D., Santa Barbara  
Discussion

10:30—**Paracervical Block in Obstetrics and Gynecology**—Clifford C. Chappell, M.D., Berkeley  
Discussion

11:00—**Management of Breech Delivery**—Richard Jonas, M.D., Newport Beach  
Discussion

11:30—**Creating the Artificial Vagina**—Frederick Naftolin, M.D., and Leo D. Lagassee, M.D., Los Angeles, both by invitation  
Discussion

9:30—Opening Remarks—George Abe, M.D., Norwalk  
9:35—Opening Remarks—Leland B. Blanchard, M.D., San Jose  
9:40—Therapeutic Modalities in Alcoholism—Max Hayman, M.D., Los Angeles  
10:00—Discussion—A. J. Malerstein, M.D., San Francisco  
10:05—Psychiatric Implications of Mutilating Surgery of the Face in Cancer Patients—David Renshaw, M.D., Santa Barbara, and Myron Feld, M.D., Long Beach, by invitation  
10:25—Discussion—Daniel S. Chaffin, M.D., San Francisco  
10:30—Status Medicamentosa—Charles W. Wahl, M.D., Los Angeles, by invitation  
10:50—Discussion—Carroll M. Brodsky, M.D., San Francisco

Members of the Panel: Wilfred Broadbent, M.D., Los Angeles, by invitation; H. Harrison Sadler, M.D., San Francisco, by invitation; George Solomon, M.D., Palo Alto; and Eugene Ziskind, M.D., Los Angeles

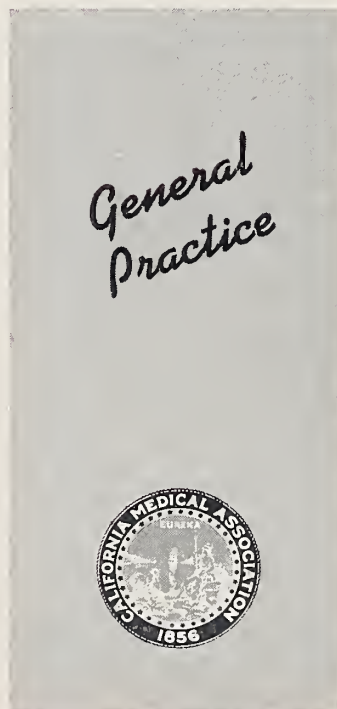
**12:15—Business Meeting**



LELAND B. BLANCHARD  
*Chairman*



J. BLAIR PACE  
*Secretary*

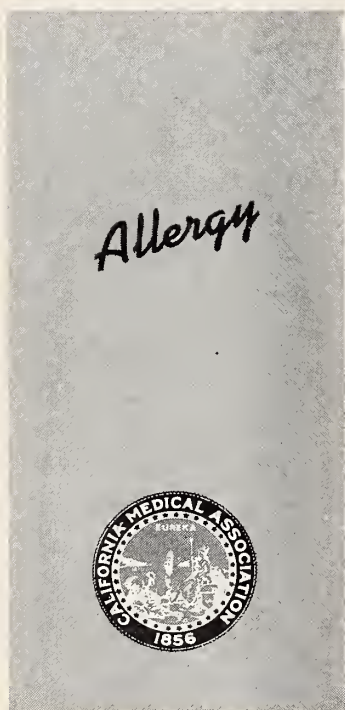




JOHN S. O'TOOLE  
Chairman



LEO N. MELEYCO  
Secretary



## ALLERGY

*Chairman*.....JOHN S. O'TOOLE, M.D., Riverside  
*Secretary*.....LEO N. MELEYCO, M.D., San Jose  
*Assistant Secretary*.....ERNEST J. SASLOW, M.D., Bakersfield

**SUNDAY, MARCH 20**      **9:00 a.m.—Rendezvous Room  
Galeria Floor**

9:00—Indications and Use of Acetylcysteine in Bronchial  
Asthma and Emphysema—Milton Millman, M.D.,  
San Diego

9:30—ACTH and Steroids: Their Use in the Practice of  
Allergy—Ralph Bookman, M.D., and Edward E.  
Katz, M.D., Los Angeles

10:00—The Effect of Beta Adrenergic Blockade on the  
Bronchial Response to Histamines and Methacholine—Gerald Zaid, M.D., Los Angeles, by invitation;  
and Gildon N. Beall, M.D., Los Angeles

10:25—Recess

10:30—Recent Concepts in the Management of Status  
Asthmaticus in Children—Warren Richards, M.D.,  
and Sheldon C. Siegel, M.D., Los Angeles

11:00—The Effects of Intermittent Steroid Therapy on  
Adrenal Responsiveness in Patients with Asthma—  
Joseph O. Young, M.D., Los Angeles, and Donald  
V. Romanaggi, M.D., Long Beach, by invitation

11:30—Yokohama Asthma—Rexford G. Haycraft, Maj.,  
M.C., USAF, Offutt Air Force Base, Offutt, Ne-  
braska, by invitation

12:00—Luncheon and Business Meeting

### Luncheon Address

The Impact of Medicare and the Casey Bill on the  
Practice of Medicine in California—Ralph Book-  
man, M.D., Los Angeles

**SUNDAY, MARCH 20**      **2:00 p.m.—Conference Room 8  
Conference Room Floor**

*Joint Meeting with the Section on Anesthesiology, the  
California Thoracic Society and the California Chapter  
of the American College of Chest Physicians*

2:00—Intrinsic Asthma—Max Samter, M.D., Chicago, by  
invitation

2:20—Chronic Bronchitis and Bronchospastic Problems—  
Gordon L. Snider, M.D., Chicago, by invitation

2:40—Inhalation Therapy and Asthmatic Problems—Le-  
Roy Misuraca, M.D., Whittier

3:00—Intensive Coronary Care and the Anesthesiologist  
—Philip R. Bromage, M.D., Montreal, by invitation

3:20—Summary and Discussion



## ANESTHESIOLOGY

*Chairman*.....BRUCE M. ANDERSON, M.D., Oakland  
*Secretary*.....THOMAS W. MCINTOSH, M.D., Pasadena  
*Assistant Secretary*.....DONALD B. DOSE, M.D., San Diego

**SUNDAY, MARCH 20      9:30 a.m.—Conference Room 8  
 Conference Room Floor**

9:30—The Anesthesiologist, the Nurse, and Narcotics—  
 Edward R. Bloomquist, M.D., Glendale

10:00—Winning Paper: California Society of Anesthesiologists Annual Competition for Residents in Anesthesiology—To be announced

10:30—Application of Dimethyl Sulfoxide in the Field of Anesthesiology—Verne L. Brechner, M.D., and David D. Cohen, M.D., Los Angeles; and Irvin Pretsky, M.D., Los Angeles, by invitation

11:00—The Role of the Anesthesiologist in Therapy—Philip R. Bromage, M.D., Montreal, by invitation

11:30—Chairman's Address—Bruce M. Anderson, M.D., Oakland

12:00—Business Meeting

**SUNDAY, MARCH 20      2:00 p.m.—Conference Room 8  
 Conference Room Floor**

*Joint Meeting with the Section on Allergy, the California Thoracic Society and the California Chapter of the American College of Chest Physicians*

2:00—Intrinsic Asthma—Max Samter, M.D., Chicago, by invitation

2:20—Chronic Bronchitis and Bronchospastic Problems—Gordon L. Snider, M.D., Chicago, by invitation

2:40—Inhalation Therapy and Asthmatic Problems—LeRoy Misuraca, M.D., Whittier

3:00—Intensive Coronary Care and the Anesthesiologist—Philip R. Bromage, M.D., Montreal, by invitation

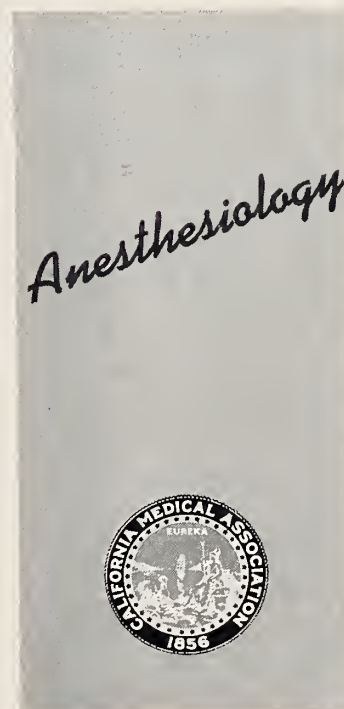
3:30—Summary and Discussion

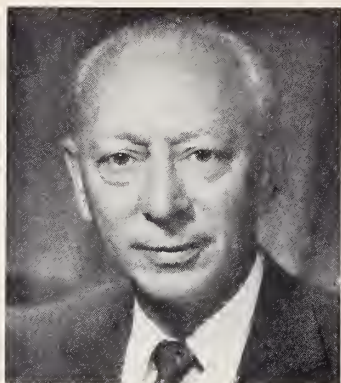


BRUCE M. ANDERSON  
*Chairman*



THOMAS W. MCINTOSH  
*Secretary*

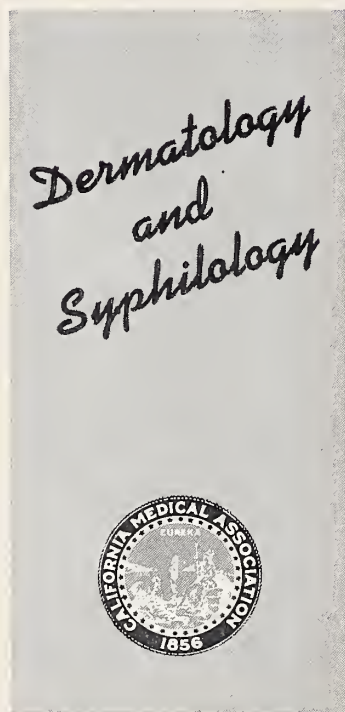




PAUL M. CROSSLAND  
Chairman



ROBERT G. WALTON  
Secretary



## DERMATOLOGY

Chairman.....PAUL M. CROSSLAND, M.D., Santa Rosa  
Secretary.....ROBERT G. WALTON, M.D., Modesto  
Assistant Secretary....SAMUEL AYRES, III, M.D., Beverly Hills

SATURDAY, MARCH 19      2:30 p.m.—Good Hope Clinic  
1241 Shatto Street

### Preconvention Meeting

*There will be a clinical meeting of the combined Los Angeles and Metropolitan Dermatological Societies at 2:30 p.m. The meeting will be held at the Good Hope Clinic, 1241 Shatto, Los Angeles. Discussion of the cases will take place at 3:30 p.m. All dermatologists are invited by the Los Angeles and Metropolitan Dermatological Societies.*

SUNDAY, MARCH 20      9:00 a.m.—Conference Room 1  
Conference Room Floor

- 9:00—Chairman's Address: Dermatological Therapy: Point and Counterpoint—Paul M. Crossland, M.D., Santa Rosa
- 9:15—The Natural History and Management of Poison Oak Dermatitis—Jonas E. Schreider, M.D., Walnut Creek
- 9:30—Immunology and Hyposensitization in Poison Oak Dermatitis—Eric E. Rosenberg, M.D., Stockton
- 9:45—Chloroquine and Electro-oculograms—Marvin Weinreb, M.D., Castro Valley
- 10:00—The Effective Control of Discoid Lupus Erythematosus with Topical Corticosteroids—Roy W. Leeper, M.D., Oakland, by invitation
- 10:15—Discussion of Preceding Papers
- 10:30—Recess
- 10:45—A Ten-Year Clinical Study and Evaluation of Therapy of Herpes Zoster at a Large General Hospital—Louis H. Winer, M.D., Beverly Hills and Edwin G. Wright, M.D., North Hollywood
- 11:00—Management of Infantile Atopic Dermatitis—Alvin H. Jacobs, M.D., San Francisco
- 11:15—Review of Neurodermatitis Emphasizing the Classification with Reference to Prognosis and Type of Therapy—Matthew J. Brunner, M.D., Pacific Palisades
- 11:30—The Management of Epidermolysis Bullosa in Children—Gerald L. Severin, M.D., Menlo Park, by invitation
- 11:45—The Treatment of Superficial Fungus Infections of the Skin—J. Walter Wilson, M.D., Los Angeles
- 12:00—Discussion of Preceding Papers
- 12:15—Recess



SUNDAY, MARCH 20      2:00 p.m.—Conference Room 1  
Conference Room Floor

- 2:00—The Treatment of Pigment of Pigmented Nevi—  
Robert G. Walton, M.D., Modesto and Alvin J. Cox,  
M.D., Palo Alto
- 2:15—Topical 5-Fluorouracil in the Treatment of Pre-  
malignant and Malignant Skin Tumors—Theodore  
A. Tromovitch, M.D., San Francisco
- 2:30—The Surgical Treatment of Rhinophyma—Walter  
E. Weber, M.D., Santa Rosa
- 2:45—Treatment of Circulatory Disorders of the Skin of  
the Lower Legs—Harold M. Schneidman, M.D., San  
Francisco
- 3:00—Discussion of Preceding Papers and Recess
- 3:15—The Local Treatment of Acne—Edward J. Ringrose,  
M.D., Berkeley
- 3:30—The Systemic Treatment of Acne—Ronald M. Reiser,  
M.D., Beverly Hills
- 3:45—The Treatment of Psoriasis in Children—Eugene  
M. Farber, M.D., Palo Alto
- 4:00—Use of Methotrexate in the Treatment of Psoriasis  
—Paul D. Foster, M.D., Los Angeles
- 4:15—Phlebotomy Therapy for Porphyria Cutanea Tarda  
Symptomata—John H. Epstein, M.D., San Francisco
- 4:30—Discussion of Preceding Papers
- 4:45—Business Meeting

#### REGISTRATION

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Galeria. *All members, guests, and visitors are requested  
to register immediately on arrival.* There is no charge  
for registration. Registration desks are open Saturday  
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will not be allowed.

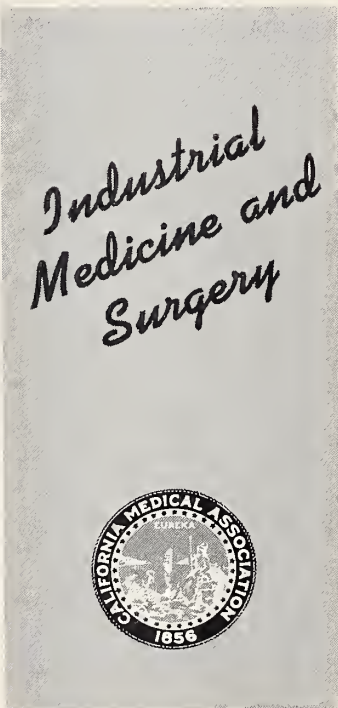
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RUFUS J. WALKER  
*Chairman*



LEON R. RUDNICK  
*Secretary*



## INDUSTRIAL MEDICINE AND SURGERY

*Chairman*.....RUFUS J. WALKER, M.D., Los Angeles  
*Secretary*.....LEON R. RUDNICK, M.D., San Leandro  
*Assistant Secretary*.....MELVIN R. PLANCEY, M.D., Los Angeles

**MONDAY, MARCH 21**      **9:30 a.m.**—Conference Room 8  
Conference Room Floor

### *Joint Meeting with the Section on Physical Medicine*

- 9:30—The Place of Cryotherapy in Daily Medical Practice  
Sedgwick Mead, M.D., Vallejo
- 10:00—An Exercise Program for Shoulder Disability—  
David Rubin, M.D., Los Angeles
- 10:30—The Exercise Program for Low Back Pain—Rene  
Cailliet, M.D., Los Angeles
- 11:00—Comparison of the Isometric and the Isotonic Ex-  
ercise Program in General Rehabilitation and  
Reconditioning—Lee C. Greene, M.D., Long Beach,  
by invitation
- 11:30—The Psychodynamics of the Compensable Injury—  
Allen J. Enelow, M.D., Los Angeles

**MONDAY, MARCH 21**      **2:00 p.m.**—Conference Room 8  
Conference Room Floor

### *Joint Meeting with Section on Physical Medicine*

- 2:00—Abbreviated History and Physical Forms to Facili-  
tate Medical Reports—Leon R. Rudnick, M.D., San  
Leandro
- 2:15—Grip Measurement on Preplacement Examination  
—H. McLeod Patterson, M.D., Fremont

### 2:30— **Panel Discussion**

#### **Exercise in the Rehabilitation of the Cardiovascular Patient**

Moderator: George C. Griffith, M.D., Los Angeles

Members of the Panel: Charles K. Friedberg, M.D., New  
York, by invitation; Robert Stivelman, M.D., and  
John H. Aldes, M.D., Los Angeles, and Myrvin H.  
Ellestad, M.D., Long Beach

4:00—Business Meeting



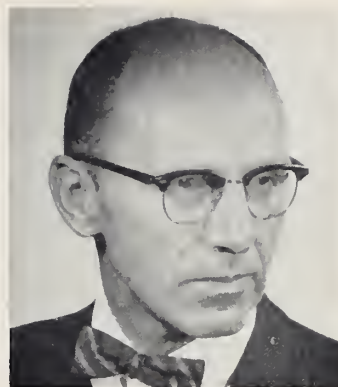
*Chairman*.....KARL L. SCHAUPP, JR., M.D., San Francisco  
*Secretary*.....LESTER T. HIBBARD, M.D., Los Angeles  
*Assistant Secretary*.....WARREN E. JONES, M.D., Sacramento

Joint Meeting with Section on General Practice  
Advances in Therapy—Obstetrics and Gynecology

11:30—Creating the Artificial Vagina—Frederick Naftolin, M.D., and Leo D. Lagassee, M.D., Los Angeles, both by invitation  
Discussion

1:00—What's New in Endocrinology—Ronald J. Pion, M.D., Seattle, by invitation

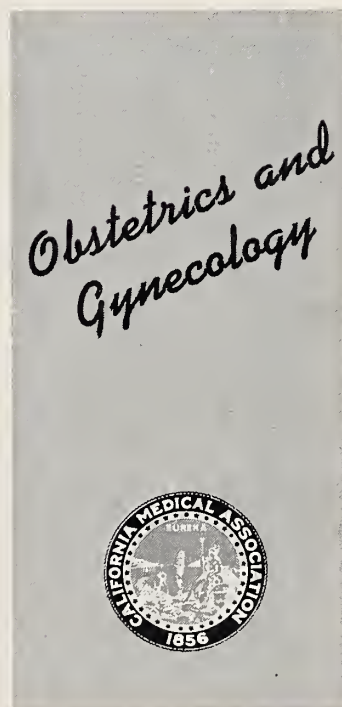
#### 4:30—Business Meeting

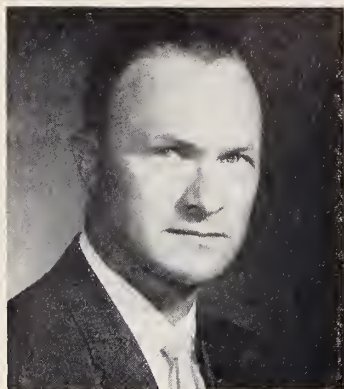


KARL L. SCHAUPP, JR.  
*Chairman*



LESTER T. HIBBARD  
*Secretary*

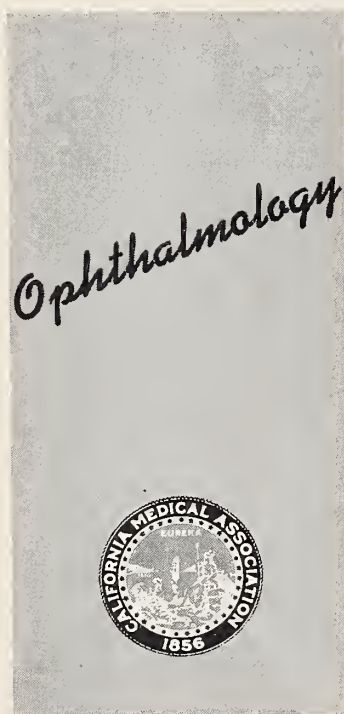




RICHARD KRATZ  
Chairman



VICTOR G. FELLOWS  
Secretary



## OPHTHALMOLOGY

Chairman.....RICHARD KRATZ, M.D., Van Nuys  
Secretary.....VICTOR G. FELLOWS, M.D., San Francisco  
Assistant Secretary.....WENDELL C. IRVINE, M.D., Los Angeles

SUNDAY, MARCH 20      2:00 p.m.—Conference Room 9  
Conference Room Floor

2:00—Newer Techniques of Lid Surgery—Alston Callahan, M.D., Birmingham, Alabama, by invitation  
Discussion

3:00—Controversial Aspects of Uveitis and Keratitis Therapy—Dan M. Gordon, M.D., New York, by invitation  
Discussion

4:00—Modern Ocular Therapeutics—Byron H. Demorest, M.D., Sacramento  
Discussion

5:00—Business Meeting

## MESSAGE CENTER

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## ORTHOPEDICS

*Chairman*.....JOHN F. COWAN, M.D., San Francisco  
*Secretary*.....DAVID C. MONSEN, M.D., Los Angeles  
*Assistant Secretary*....ARTHUR R. HARTWIG, M.D., San Francisco

**SUNDAY, MARCH 20    9:15 a.m.—Conference Room 10  
Conference Room Floor**



JOHN F. COWAN  
*Chairman*



DAVID C. MONSEN  
*Secretary*

9:15—An Additional Method for the Management of the Orthopedic Infection—Floyd H. Jergesen, M.D., San Francisco, and Paul M. Lagomarsino, M.D., San Francisco, by invitation

9:35—Tendon Transfers in the Child with Cerebral Palsy—Robert L. Samilson, M.D., San Francisco

9:55—Observations of the Hanging Hip—Max Scheck, M.D., San Francisco

10:15—Recess

10:30— **Panel Discussion**

**Lumbar Laminectomy or Fusion or Both**

Moderator: John F. Cowan, M.D., San Francisco

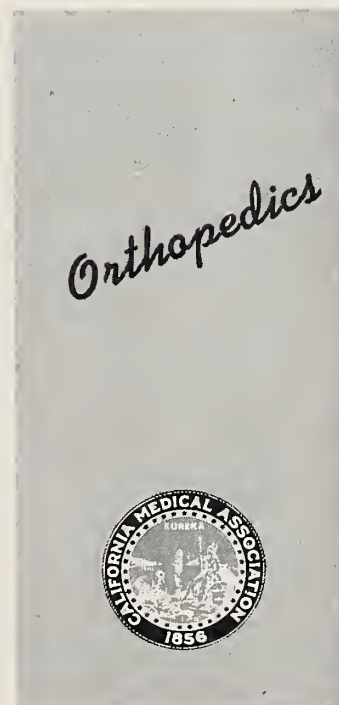
Members of the Panel: Alonzo J. Neufeld, M.D., Homer C. Pheasant, M.D., Los Angeles, H. Mason Hohl, M.D., Beverly Hills, Leon L. Wiltse, M.D., Long Beach, and Ellis W. Jones, M.D., Pasadena

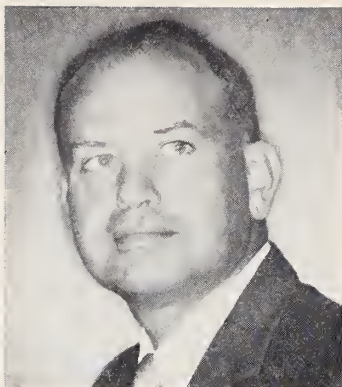
12:00—Business Meeting

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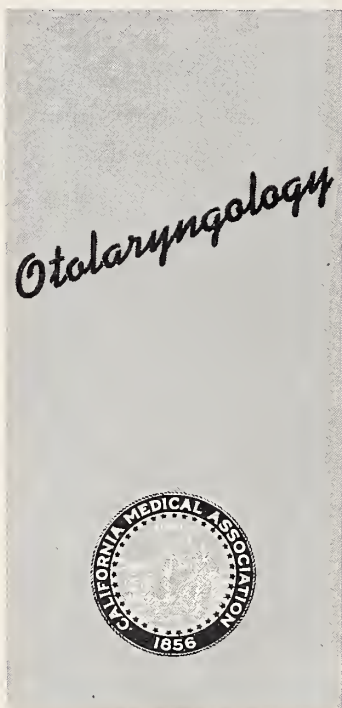




THOMAS L. SOSS  
Chairman



G. HOWARD GOTTSCHALK  
Secretary



## OTOLARYNGOLOGY

*Chairman*.....THOMAS L. SOSS, M.D., San Mateo  
*Secretary*.....G. HOWARD GOTTSCHALK, M.D., Los Angeles  
*Assistant Secretary*.....CHARLES P. LEBO, M.D., San Francisco

**SUNDAY, MARCH 20**      **9:30 a.m.—Conference Room 9**  
Conference Room Floor

**9:30—Office Management of the Chronically Draining Ear**  
—James L. Sheehy, M.D., Los Angeles  
Discussion

**9:55—Anti-inflammatory Agents in Facial Plastic Surgery**  
—Byron J. Bailey, M.D., Torrance  
Discussion

**10:20—Traumatic Subglottic Stenosis, Surgical Treatment**  
Including a Report of Two Cases—Irving L. White,  
M.D., Long Beach  
Discussion

**10:45—The Use of Estrogens in Otolaryngology—Maurice**  
Schiff, M.D., Escondido  
Discussion

**11:10—Tomography of the Ear in Surgically Correctable**  
Hearing Loss—Leon G. Kaseff, M.D., San Francisco  
Discussion

**11:35—Business Meeting**

## QUALIFICATIONS/REQUIREMENTS FOR REGISTRATION

(a) All M.D.'s with credentials showing that they hold valid license to practice medicine. (Membership card in C.M.A.; county medical society/association or A.M.A. membership card.)

(b) Medical students will be admitted upon presentation of credentials from their medical schools identifying them as medical students. (A membership card of the Student American Medical Association or letter from their dean's office.)

(c) Medical assistants will be admitted upon presentation of a letter from the physician-employer or C.M.A.A. membership card.

(d) Military paramedical personnel will be admitted upon presentation of a letter requesting their admittance, written by their commanding officer.

(e) Dentists (D.D.S.), doctors of veterinary medicine (D.V.M.), registered nurses (R.N.), student nurses, x-ray technicians, laboratory technicians, allied public health personnel, and others will be admitted provided they have proper identification.

(f) All questions an admission will be passed upon by a member of the Committee on Registration who will be present at the desk.



## **PATHOLOGY**

*Chairman*.....WILLIAM C. HERRICK, M.D., San Diego  
*Secretary*.....FRANK R. DUTRA, M.D., Castro Valley  
*Assistant Secretary*.....WILLIAM H. KERN, M.D., Los Angeles

**SATURDAY, MARCH 19 9:00 a.m.—Conference Room 4  
Conference Room Floor**

Moderator: William C. Herrick, M.D., San Diego

9:00 a.m. to 12 Noon—Contributed Papers

See Official Program, distributed at the time  
of registration, for detailed program.

**SATURDAY, MARCH 19 2:00 p.m.—Conference Room 4  
Conference Room Floor**

2:00 p.m. to 5:00 p.m.—Business Meeting

**SUNDAY, MARCH 20 9:00 a.m.—Galeria Room  
Galeria Floor**

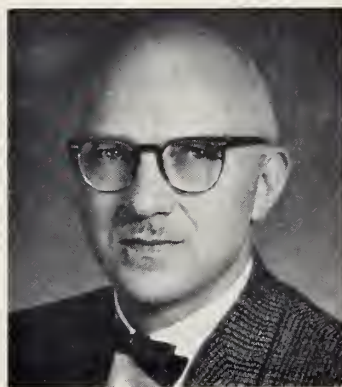
### **Seminar on Electrolytes**

Moderator: William C. Herrick, M.D., San Diego

Members of the Panel: Daniel Baer, M.D., Portland, Oregon, by invitation; and others to be announced



WILLIAM C. HERRICK  
*Chairman*



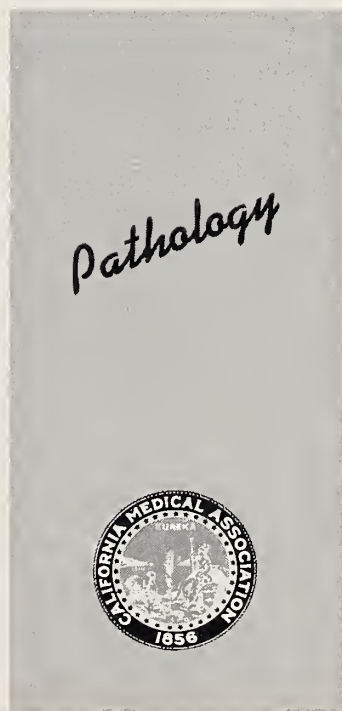
FRANK R. DUTRA  
*Secretary*

## **EMERGENCY CALLS AND MESSAGES**

Convention Emergency Call Number 213 629-6416

8:30 a.m. to 4:30 p.m.

Saturday March 19 to Wednesday, March 23

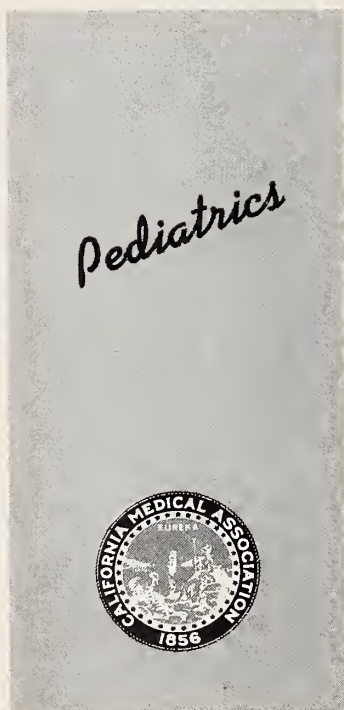




JACK W. BILLS  
*Chairman*



RICHARD L. ANDERSON  
*Secretary*



## PEDIATRICS

*Chairman*.....JACK W. BILLS, M.D., Van Nuys  
*Secretary*.....RICHARD L. ANDERSON, M.D., Eureka  
*Assistant Secretary*.....SHERROD C. SWIFT, M.D., Whittier

**SUNDAY, MARCH 20      9:00 a.m.—Conference Room 4  
Conference Room Floor**

The program presented by the Pediatric Section of the California Medical Association this year is a departure from the strictly scientific programs offered in previous years. We have invited guests from state and federal government agencies which render service to, or are directly concerned with the doctors who are involved with the care of infants, children, and adolescents in all aspects. The sums of money that are and that will become available through these various agencies are enormous and will become a much more important segment of our individual and joint practices, not so much with regard to the monetary return, but from the increasing numbers of patients involved who are eligible for study and care.

It is of paramount importance for each of us to be as familiar as possible with all the available services for our patients.

**SUNDAY, MARCH 20      9:00 a.m.—Conference Room 4  
Conference Room Floor**

9:00—American Academy of Pediatrics—Reported by E. H. Christopherson, M.D., Executive Director, Evanston, Illinois, by invitation

9:20—Crippled Children Services, California State Department of Public Health—Reported by Ralph Hornberger, M.D., Chief of Service, Berkeley

9:50—Bureau of Maternal and Child Health, California State Department of Public Health—Reported by Robert Day, M.D., Chief of Bureau, Berkeley

10:10—Bureau of Mental Retardation Service, California State Department of Public Health—Reported by Charles Gardipee, M.D., Chief of Bureau, Berkeley

10:30—Recess

10:45—Children's Bureau Projects, Children's Bureau, United States Department of Health, Education and Welfare—Reported by John J. Hutchings, M.D., Regional Medical Consultant on Mental Retardation, San Francisco

11:10—Medical Care Division, California Department of Social Welfare—Reported by Lester E. McDonald, M.D., Medical Consultant, Sacramento, by invitation

11:30—Family and Children's Division, California Department of Social Welfare—Reported by Miss Lucille Kennedy, Chief of Division, Sacramento, by invitation



11:45—California Department of Mental Hygiene—Reported by William B. Beach, Jr., M.D., Deputy Director, Sacramento

12:00—Vocational Rehabilitation of Adolescents, California Department of Vocational Rehabilitation—Reported by Mr. Donald Blyth, Regional Administrator of Southern California, Los Angeles, by invitation

**SUNDAY, MARCH 20      12:30 p.m.—Conference Room 4  
Conference Room Floor**

12:30—Pediatricians' Luncheon and Question and Answer Period. Advance reservations are necessary, and may be made with Sherrod C. Swift, M.D., 14619 Whittier Boulevard, Whittier. Price \$6.00

2:00—Business Meeting

2:30—Business Meeting of the Council of Pediatric Societies

### **QUALIFICATIONS/REQUIREMENTS FOR REGISTRATION**

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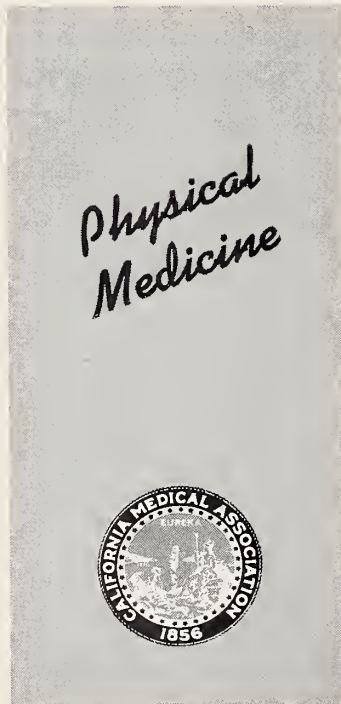
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GREGORY BARD  
*Chairman*



RENE CAILLIET  
*Secretary*



## PHYSICAL MEDICINE

*Chairman*.....GREGORY BARD, M.D., San Francisco  
*Secretary*.....RENE CAILLIET, M.D., Los Angeles  
*Assistant Secretary*.....ANTON TRATAR, M.D., San Francisco

**MONDAY, MARCH 21      9:30 a.m.—Conference Room 8  
Conference Room Floor**

### *Joint Meeting with Section on Industrial Medicine and Surgery*

- 9:30—The Place of Cryotherapy in Daily Medical Practice—  
Sedgwick Mead, M.D., Vallejo
- 10:00—An Exercise Program for Shoulder Disability—  
David Rubin, M.D., Los Angeles
- 10:30—The Exercise Program for Low Back Pain—Rene  
Cailliet, M.D., Los Angeles
- 11:00—Comparison of the Isometric and the Isotonic Ex-  
ercise Program in General Rehabilitation and Re-  
conditioning—Lee C. Greene, M.D., Long Beach, by  
invitation
- 11:30—The Psychodynamics of Compensable Injury—Allen  
J. Enelow, M.D., Los Angeles

**MONDAY, MARCH 21      2:00 p.m.—Conference Room 8  
Conference Room Floor**

### *Joint Meeting with Section on Industrial Medicine and Surgery*

- 2:00—Abbreviated History and Physical Forms to Facili-  
tate Medical Reports—Leon R. Rudnick, M.D., San  
Leandro
- 2:15—Grip Measurement on Preplacement Examination  
—H. McLeod Patterson, M.D., Fremont

### 2:30— **Panel Discussion**

#### **Exercise in the Rehabilitation of the Cardiovascular Patient**

Moderator: George C. Griffith, M.D., Los Angeles

Members of the Panel: Charles K. Friedberg, M.D., New  
York, by invitation; Robert Stivelman, M.D., and  
John H. Aldes, M.D., Los Angeles; and Myrvin H.  
Ellestad, M.D., Long Beach

4:00—Business Meeting

**VISIT SCIENTIFIC AND  
TECHNICAL EXHIBITS**



## PREVENTIVE MEDICINE AND PUBLIC HEALTH

*Chairman*.....BYRON O. MORK, M.D., San Diego  
*Secretary*.....HENRIK L. BLUM, M.D., Martinez  
*Assistant Secretary*..HERBERT H. COWPER,\* M.D., Los Angeles

\*Deceased

**MONDAY, MARCH 21**      **1:30 p.m.—Conference Room 4**  
Conference Room Floor

1:30—An Evaluation of a Streptococcal Disease Prevention Program—Donald C. Fyler, M.D., Los Angeles  
Discussion—Edward L. Russell, M.D., Santa Ana

2:00—The Physician and Community Services for Cardiovascular Disease Control—J. Gordon Barrow, M.D., Atlanta, by invitation  
Discussion

2:45—Recess

2:50—A New Screening Test for Syphilis: The Latex Serologic Test for Syphilis—Charles M. Carpenter, Los Angeles; Isobella Konya, B.S., and Ronald H. LeClaire, M.S., Los Angeles, both by invitation

3:10—A Future for Preventive Medicine—Lester Breslow, M.D., Berkeley

3:45— **Panel Discussion**

Continuity of Care—Hospital, Long-term Care Facility

Moderator: Pierre J. Salmon, M.D., San Mateo

Members of the Panel: Mr. Robert Burness and Mrs. Inge Lingemann, R.N., San Mateo, by invitation

4:45—Business Meeting



BYRON O. MORK  
*Chairman*



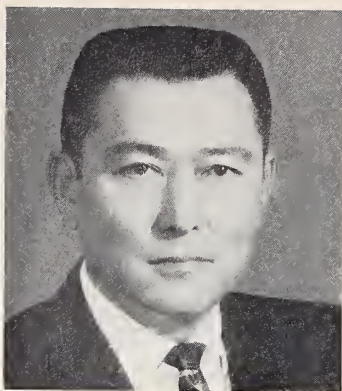
HENRIK L. BLUM  
*Secretary*

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*Preventive  
Medicine and  
Public Health*

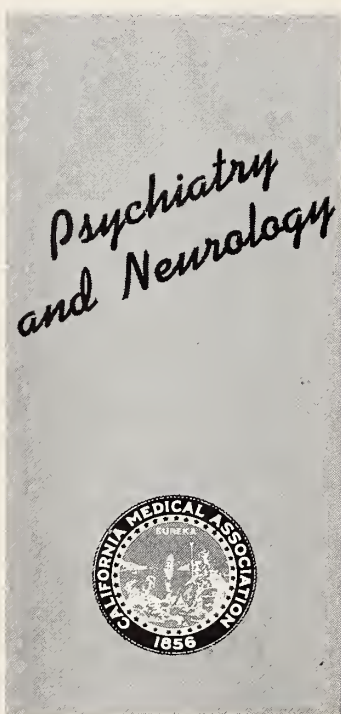




GEORGE Y. ABE  
Chairman



WERNER M. MENDEL  
Secretary



## PSYCHIATRY AND NEUROLOGY

Chairman.....GEORGE Y. ABE, M.D., Norwalk  
Secretary.....WERNER M. MENDEL, M.D., Los Angeles  
Assistant Secretary.....AMES FISCHER, M.D., San Francisco

WEDNESDAY, MARCH 23

9:30 a.m.—Galeria Room  
Galeria Floor

Joint Meeting with the Section on General Practice

9:30—Opening Remarks—George Abe, M.D., Norwalk

9:35—Opening Remarks—Leland B. Blanchard, M.D., San Jose

9:40—Therapeutic Modalities in Alcoholism—Max Hayman, M.D., Los Angeles

10:00—Discussion—A. J. Malerstein, M.D., San Francisco

10:05—Psychiatric Implications of Mutilating Surgery of the Face in Cancer Patients—David Renshaw, M.D., Santa Barbara; and Myron Feld, M.D., Long Beach, by invitation

10:25—Discussion—Daniel S. Chaffin, M.D., San Francisco

10:30—Status Medicamentosa—Charles W. Wahl, M.D., Los Angeles, by invitation

10:50—Discussion—Carroll M. Brodsky, M.D., San Francisco

11:00— **Panel Discussion**

Concepts of Psychosomatic Disease—1966

Moderator: Allen J. Enelow, M.D., Los Angeles

Members of the Panel: Wilfred Broadbent, M.D., Los Angeles, by invitation; H. Harrison Sadler, M.D., San Francisco, by invitation; George Solomon, M.D., Palo Alto; and Eugene Ziskind, M.D., Los Angeles

12:15—Business Meeting

WEDNESDAY, MARCH 23

2:00 p.m.—Galeria Room  
Galeria Floor

2:00—Opening Remarks—Howard S. Barrows, M.D., Los Angeles

2:05—The Chronic Meningitides—Ruth A. McCormick, M.D., Los Angeles

2:30—Discussion

2:40—The Electroencephalogram in Behavior Disorders in Children—Robert N. Pavy, M.D., and William Anderson, M.D., San Mateo

3:05—Discussion

3:15—Recess

3:25—Aphasia Testing at the Bedside—Robert Tager, M.D., Los Angeles, by invitation

3:50—Discussion



## RADIOLOGY

*Chairman*.....JOHN C. BENNETT, M.D., San Francisco  
*Secretary*.....VICTOR G. MIKITY, M.D., Los Angeles  
*Assistant Secretary*.....VERNON R. GEE, M.D., Redding

**SUNDAY, MARCH 20**      9:30 a.m.—Conference Room 2  
Conference Room Floor

9:30—Radiographic Detection of Polyethylene Catheter Embolus—David R. Coblentz, M.D., Los Angeles, by invitation

9:50—Roentgen Findings in Occipital Tumors—William N. Hanafée, M.D., and Larry P. Bilodeau, M.D., Los Angeles

10:10—Amplifier-guided Needle Aspiration Biopsy of Lung Lesions—G. Melvin Stevens, M.D., Palo Alto

10:30—                      **Panel Discussion**

Voiding Cystourethrography in Children

Moderator: Victor G. Mikity, M.D., Los Angeles

Members of the Panel: John B. James, M.D., El Monte; and Harold H. Edelbrock, M.D., Hollywood

11:30—A Surgical Miscellany—Owen H. Wangenstein, M.D., Minneapolis, by invitation

12:15—Business Meeting

**SUNDAY, MARCH 20**      1:30 p.m.—Conference Room 2  
Conference Room Floor

1:30—Hyperbaric Irradiation Therapy: Theory and Practice—Melville L. Jacobs, M.D., Duarte

2:00—Radiation Therapy: Carcinoma of the Bladder—George A. Jack, M.D., San Francisco, by invitation; and Franz Buschke, M.D., San Francisco

2:20—Radiation Therapy in Myasthenia Gravis—Theodore Phillips, M.D., San Francisco, by invitation; and Franz Buschke, M.D., San Francisco

2:40—Meet John Doe, Radiologist—Vernon R. Gee, M.D., Redding

3:00—Recess—Annual Meeting of California Radiological Society

## EMERGENCY CALLS AND MESSAGES

Convention Emergency Call Number 213 629-6416

8:30 a.m. to 4:30 p.m.

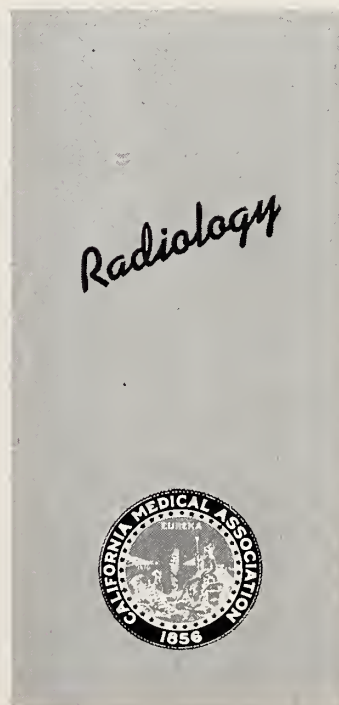
Saturday March 19 to Wednesday, March 23



JOHN C. BENNETT  
*Chairman*



VICTOR G. MIKITY  
*Secretary*

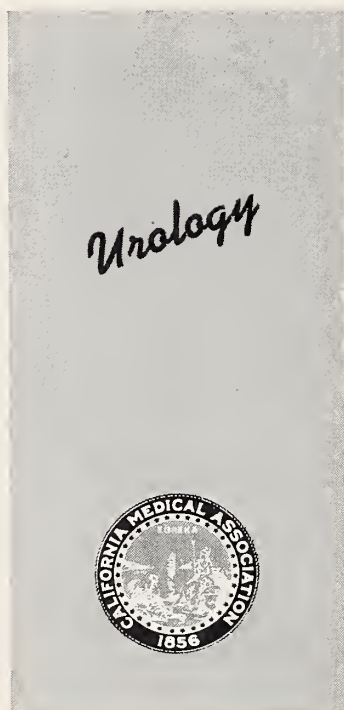




CARL BURKLAND  
Chairman



CARL K. PEARLMAN  
Secretary



## UROLOGY

*Chairman*.....CARL BURKLAND, M.D., Sacramento  
*Secretary*.....CARL K. PEARLMAN, M.D., Santa Ana  
*Assistant Secretary*.....JAMES L. GOEBEL, M.D., Ross

### TUESDAY, MARCH 22 10:30 a.m.\*—Conference Room 2 Conference Room Floor

- 10:30—Bladder Tumor Diagnosis with Double Dose Contrast Median, Excretory Cystogram—Arjan D. Amar, M.D., Walnut Creek
- 10:45—Discussant—Henry M. Weyrauch, M.D., San Francisco
- 10:50—Diagnosis and Treatment of Urinary Tract Infections in the Female—John M. Palmer, M.D., Palo Alto, by invitation, and Thomas A. Stamey, M.D., Palo Alto
- 11:20—Urinary Tract Infection in Children with Distal Urethral Stenosis—Robert A. Bridge, M.D., San Diego
- 11:35—Discussants—Richards P. Lyon, M.D., Berkeley, and Harold H. Edlebrock, M.D., Hollywood
- 11:40—Peritoneal Dialysis: A Simple Useful Procedure for the Management of Renal Failure—Charles F. Humphreys, M.D., Berkeley

### TUESDAY, MARCH 22 1:30 p.m.—Conference Room 2 Conference Room Floor

- 1:30—Review of Prostatectomy in a County Hospital: Comparison with a Private Series—The Third of a Trilogy—Robert J. Prentiss, M.D., San Diego, and John W. Pennington, M.D., San Diego, by invitation
- 1:45—Discussant—Milo Ellick, M.D., Long Beach
- 2:10—Chairman's Address—The Hazards of Being a Male: Emphasis on Urogenital Factors—Carl E. Burkland, M.D., Sacramento
- 2:25—Business Meeting
- 2:40—Recess
- 2:45—Combining Surgery for Ureterocele with Uretrovesicoplasty to Prevent Postoperative Reflux—John A. Hutch, M.D., and Eugene R. Chisholm, M.D., Pleasant Hill
- 3:00—Discussant—Paul L. Getzoff, M.D., Beverly Hills

\*Attention of the members of the Urology Section is directed to the Third General Meeting on Chronic Renal Failure, Tuesday, March 22, 9:00 a.m., Ballroom.



- 3:05—External Radiation: A Successful Modality in Preventing Hormonally Induced Gynecomastia—Thomas E. Shown, Capt., M.C., U.S.A.; Mauro P. Gangai, Maj., M.C., U.S.A.; Paul E. Sieber, Col., M.C., U.S.A.; and Charles A. Moore, Lt. Col., M.C., U.S.A.; San Francisco, all by invitation
- 3:20—Tetracycline Fluorescence in Urinary Tract Tumors—Samuel Kunin, M.D., and S. F. Cooper, M.D., Los Angeles, both by invitation
- 3:35—A Ten-Year Survival Following Cystectomy and Lymphadenectomy for High-Grade Carcinoma of the Bladder—Jay R. Longley, M.D., Newport Beach, and Bernard Mason, M.D., Huntington Beach
- 3:50—Regression and Control of Metastatic Renal Cancer—Matlock M. Mims, M. D., Los Angeles
- 4:05—Discussants—Abraham T. Cockett, M.D., Torrance, and Gordon L. Verity, M.D., San Diego

#### ACKNOWLEDMENT

A major objective of the Scientific Board in recent years has been the improvement of the Annual Scientific Assembly. The progress towards the attainment of this objective has been made possible by the work of many physicians, and the support of sections, committees, specialty societies and voluntary health agencies. Lack of space prevents the listing of these people and groups, but the California Medical Association is extremely appreciative of their cooperation.

Committee on Scientific Assemblies  
of the Scientific Board

VICTOR RICHARDS, M.D., *Chairman*

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## COLOR TELEVISION PROGRAM

Music Room • Biltmore Hotel

### PLANNING COMMITTEE

William D. Evans, M.D., Chairman

Sol Bernstein, M.D.

Margaret M. McCarron, M.D.

Bernard J. O'Loughlin, M.D.

Closed Circuit Television programs will be offered Monday, Tuesday and Wednesday in the Music Room, Biltmore Hotel. Each program will have a Moderator and Panel of Discussants present at the Biltmore Hotel with operative procedures and patient interviews or demonstrations televised from Los Angeles County General Hospital. Following is a list of the programs. The complete Color Television Program giving descriptions and listings of moderators, surgeons, demonstrators, and panels will be available at the Registration Desk at the time of the meeting.

## MOTION PICTURE PROGRAM

Music Room • Biltmore Hotel

### Co-Chairmen:

Richard E. Gardner, M.D.

W. Morris H. Noble, M.D.

Four film symposia will be presented, each utilizing about two-thirds of the time for projection of films, and one-third for discussions, questions and answers.

Be sure to read the **SPECIAL MOTION PICTURE PROGRAM** distributed at the time of registration with complete listing of films, descriptions, moderators, discussants and time schedules.

### MONDAY, MARCH 21

9:00 a.m. to 12 noon

9:00 a.m.— DIABETES: LESIONS AND LESSONS

Moderator: Helen E. Martin, M.D., Los Angeles

10:30 a.m.— NEUROLOGICAL EXAMINATION

Moderator: Ruth A. McCormick, M.D., Los Angeles

Demonstrator: Howard S. Barrows, M.D., Los Angeles

### TUESDAY, MARCH 22

2:00 p.m. to 5:00 p.m.

2:00 p.m.— COLONIC RESECTION

Moderator: Arthur J. Donovan, M.D., Los Angeles

Surgeon: Clarence J. Berne, M.D., Los Angeles

### WEDNESDAY, MARCH 23

9:00 a.m. to 12 noon

9:00 a.m.— CENTRAL NERVOUS SYSTEM INFECTIONS

Moderator: Paul F. Wehrle, M.D., Los Angeles

10:30 a.m.— DERMATOLOGY CLINIC

Co-Moderators: Norman Levan, M.D., Los Angeles

Marjorie F. Bauer, M.D., Los Angeles

Ben A. Newman, M.D., Beverly Hills

### SUNDAY, MARCH 20

9:00 a.m. to 12:00 noon

#### SURGERY

Moderator: Richard E. Gardner, M.D., San Francisco

A New Look at Tetanus Prophylaxis

Diseases of the Gallbladder

Long-Term Cannulation for Hemodialysis

A Stereotaxic Method for Investigation and Treatment of Involuntary Movements and Intractable Pain

### MONDAY, MARCH 21

2:00 p.m. to 5:00 p.m.

#### MEDICINE

Moderator: W. Morris H. Noble, M.D., San Francisco

Bronchitis—A Team Affair

I've Been Living with Gout

Cardioversion During the Awake State

### TUESDAY, MARCH 22

9:00 a.m. to 1:30 p.m.

9:00 a.m.— RADIATION

Moderator: Justin Stein, M.D., Los Angeles

Heavy Particle Radiation

Acromegaly: Diagnosis, Etiology, Therapy

Radiation: Physician and Patient

12:30 p.m.— LASER BEAM

Moderator: James T. Helsper, M.D., Pasadena

Laser and Living Cells

Laser Beam Therapy

### WEDNESDAY, MARCH 23

2:00 p.m. to 5:00 p.m.

#### GENERAL PROGRAM

Moderator: Clarence T. Halburg, M.D., Redlands

Low Cervical Cesarean Section—Transverse Uterine Incision

Why Blood Volume?

Clinical Applanation Tonometry with the Goldman Tonometer

The Long-Term Use of Anticoagulants



# SCIENTIFIC AND ORGANIZATIONAL EXHIBITS

## *Scientific Exhibits*

Rex Room, Below Biltmore Bowl

**The Physiochemical Rational in the Treatment of Shock**—William Schumer, M.D., Sacramento, by invitation. This exhibit is a visual explanation of the newer biochemical and physiological rationale in the treatment of shock. It consists of three sections: (1) Microphotographs of the microcirculation of the dog as it is bled to shock levels. A flow diagram explains the physiological compensation and biochemical complications which are produced by shock. (2) Cinemicrophotographs, stills of the microcirculation, metabolic study and survival rate charts, and metabolic flow diagrams illustrate the technique utilized in experimental production of shock and the effect lactic acid, 1-norepinephrine, and vasodilators (nitrates) have on the microcirculation and the cellular metabolism. (3) Summary of the exhibit supports the use of vasodilatory over vasoconstrictive therapy in shock, and proves that vasodilators increase tissue perfusion and decrease lactic acidosis.

**Cryosurgery of Head and Neck**—Robert Rand, M.D., and Hans von Leden, M.D., Hollywood. This exhibit will consist of illustrations, equipment and signs. The techniques, tissue changes and the advantages and disadvantages of cryo surgery will be shown.

**The Potassium-Induced Circumferential Small Bowel Ulcer**—Leon Morgenstern, M.D., Joel Panish, M.D., Los Angeles, and Michael Freilich, M.D., Los Angeles, by invitation. The clinical and pathologic characteristics of the circumferential small bowel ulcer associated with thiazide-potassium medication have now been clearly delineated in reports from this and other institutions. Since 1960 we have been collecting material on this unusual entity, and now have 25 cases which have undergone surgical resection. During the course of these past five years we have accumulated a wealth of excellent illustrative material in the operating room and in the pathology laboratory. It is this material, in large color transparencies, which will be shown in the exhibit. Also to be shown are several permanently mounted actual gross specimens embedded in plastic. A brief text in outline accompanies the various portions of the exhibit, giving the viewer a clear, concise summary of the disease.

The final section depicts the experimental results in duplicating the lesion and presents a series of conclusions based on the clinical and laboratory material.

**Diagnostic Testing Unit on Hypertensive Diseases**—California Heart Association—Harold I. Griffeath, M.D., San Francisco. The exhibit consists of two self-illuminated panels giving two medical cases with x-rays, photographs of eyegrounds, and sets of eight electrocardiograms. These are correlated with written case histories, and a multiple choice questionnaire.

**Clinical Potassium Deficit**—W. D. Snively, Jr., M.D., and R. L. Westerman, M.D., Evansville, Indiana, by invitation. This exhibit presents the salient facts concerning potassium deficit in clinical medicine, emphasizing that this deficit—hazardous if allowed to continue—can be easily prevented, readily detected, and effectively treated.

Results of studies showing the high incidence of potassium deficit, both in in-patients and out-patients, will be highlighted graphically. Causes of potassium deficit will be demonstrated pictorially, as will the physiologic mechanisms by which deficits occur. Symptoms and physical findings in mild to severe potassium deficit will be visually demonstrated. Advantages and disadvantages of various salts of potassium will be covered. Therapy will emphasize that potassium deficit is a cellular deficit.

**Reduction of Unnecessary Medical X-ray Exposure(s)**—Simon Kinsman, Ph.D., Sacramento, by invitation. An x-ray generator will be set up to radiograph a phantom in a cubicle shielded on five sides. Radiation detection instruments will be placed at several locations. The visitors can measure (read instrument dials) the scattered radiation for various settings of kilovoltage, milliamperage, filter thickness, and beam restricters.

**The Sounds of Venous Air Embolism**—Charles C. Wycoff, M.D., and John E. Cann, M.D., San Francisco. This exhibit is a continuation of an exhibit at the 1965 Annual Scientific Assembly of the California Medical Association. A continuously running tape-recorder will reproduce the heart sounds of systemic air embolism in the dog. There will be charts of the variation of blood pressure and arterial oxygen tension as well as records of the electrocardiogram. A refinement of the 1965 demonstration will be made. This demonstration is designed to augment a scientific paper to be presented at the same meeting.

## *Organizational Exhibits*

South Galeria, Galeria Floor

**California Medical Association Physician Placement Service**—The Coordinator of the Physician Placement Service will be on hand throughout the meeting to discuss opportunities for practice in California, and to assist those having openings they wish to list in the Placement Bulletin.

**Medicine and Religion**—The Committee on Medicine and Religion, California Medical Association. The purpose of this exhibit is to stimulate interest and offer assistance to county medical societies.

(Continued on next page)

**Food and Drug Administration: Adverse Drug Registry**—The exhibit shows location of cooperating hospitals, methods of collection and distribution of information on reactions. The cooperation of the Food and Drug Administration and the American Medical Association is stressed.

**American Medical Association: Adverse Drug Registry**—The purpose of this exhibit is to inform physicians of the American Medical Association Registry, to encourage their participation, and to stress the importance of drug associated reactions. The exhibit contains illustrations of specific drug reactions, and their causes and visual requests for reporting of reactions.

**American Medical Association: Occupational Health**—A permanent display of 60 publications, any of which may be ordered without charge. In addition, three publications will be available as hand-outs at the exhibit.

**American Medical Association: Nutrition**—This exhibit indicates the sources and importance of dietary fats; it points out indications and recom-

mendations for modifying dietary fat; it lists in graph form the total fat and the polyunsaturated fat content of foods.

**State Department of Public Health: Tumor Registry**—A series of charts and graphs giving the distribution in man of cancer by site, state of disease at diagnosis and survival rate.

**California Medical Association: Committee on Maternal and Child Care**—The results of a two-year study of all fatal cases of Hemolytic Diseases of the Newborn are reviewed, listing frequencies of avoidable factors, physician and laboratory. Recommendations for improvement of HDN management are given.

**How To Approach the Eye**—Dan M. Gordon, M.D., New York, by invitation. The exhibit will cover the fundamentals of an eye-examination—stressing the conditions which the non-ophthalmologist can and cannot handle, illustrating important diagnostic hints. The differentiation between conjunctival and ciliary injections will be illustrated as well as indications for the use of anti-inflammatory agents with or without antimicrobials. A sample eye tray will be shown.

## QUALIFICATIONS/REQUIREMENTS FOR REGISTRATION

(a) All M.D.'s with credentials showing that they hold valid license to practice medicine. (Membership card in C.M.A.; county medical society/association or A.M.A. membership card.)

(b) Medical students will be admitted upon presentation of credentials from their medical schools identifying them as medical students. (A membership card of the Student American Medical Association or letter from their dean's office.)

(c) Medical assistants will be admitted upon presentation of a letter from the physician-employer or C.M.A.A. membership card.

(d) Military paramedical personnel will be admitted upon presentation of a letter requesting their admittance, written by their commanding officer.

(e) Dentists (D.D.S.), doctors of veterinary medicine (D.V.M.), registered nurses (R.N.), student nurses, x-ray technicians, laboratory technicians, allied public health personnel, and others will be admitted provided they have proper identification.

(f) All questions on admission will be passed upon by a member of the Committee on Registration who will be present at the desk.



# WOMAN'S AUXILIARY

## THIRTY-SIXTH ANNUAL CONVENTION

MARCH 20 to 23, 1966

Headquarters: Biltmore Hotel, Los Angeles

Convention Chairman: MRS. WILLIAM F. ROE

Convention Co-Chairman: MRS. EUGENE E. CAHILL

### REGISTRATION—North Galeria

Sunday, March 20—9:00 a.m. to 4:00 p.m.

Monday, March 21—8:00 a.m. to 4:00 p.m.

Tuesday, March 22—8:30 a.m. to Noon

### SATURDAY, March 19

7:00 p.m.—Annual Report of Woman's Auxiliary presented by the President, Mrs. George J. Bower, to the California Medical Association House of Delegates, Biltmore Bowl. Doctors' wives are invited to attend. Auxiliary members will not register for this meeting. Woman's Auxiliary Registration will start Sunday morning

### SUNDAY, March 20

9:00 a.m.—Executive Committee breakfast meeting, President's Suite

2:30 p.m.—Pre-Convention Board meeting, Conference Room #5

### MONDAY, March 21

8:30 a.m.—Opening Session of House of Delegates, Biltmore Bowl

11:15 a.m.—“Pronto” Luncheon to be served in Biltmore Bowl

12:45 p.m.—Afternoon Session of House of Delegates, Biltmore Bowl

### TUESDAY, March 22

8:30 a.m.—Final Session of the House of Delegates, Biltmore Bowl

12:15 to 1:00 p.m.—Reception honoring incoming and outgoing officers, Ballroom Foyer

1:00 p.m.—Presidents' Luncheon honoring Mrs. George J. Bower and Mrs. Samuel K. Bacon, President-Elect; State Past Presidents; and CMA Advisory Board and their wives, Ballroom

### WEDNESDAY, March 23

8:00 a.m.—Post-Convention Board meeting, Mrs. Samuel K. Bacon presiding, Conference Room 4

9:00 a.m.—Orientation Meeting for 1966-67 State Board Members, District Councilors, County and District Presidents. Incoming County Board Members are also welcome. Mrs. Samuel K. Bacon presiding, Conference Room #4

### HOSPITALITY CENTER

The Hospitality Center will be open

Sunday, March 20—12:00 to 4:00 p.m.

Monday, March 21—9:00 a.m. to 5:00 p.m.

Tuesday, March 22—9:00 a.m. to Noon



MRS. GEORGE J. BOWER, *President*



MRS. SAMUEL K. BACON, *President-Elect*

# OFFICERS AND DELEGATES

## General Officers

Ralph C. Teall, Sacramento.....*President*  
 James C. MacLaggan, San Diego.....*President-Elect*  
 William F. Quinn, Los Angeles.....*Speaker of House of Delegates*  
 Joseph W. Telford, San Diego....*Vice-Speaker of House of Delegates*  
 Carl E. Anderson, Santa Rosa.....*Chairman of Council*  
 Matthew N. Hosmer, San Francisco.....*Secretary*  
 Dwight L. Wilbur, San Francisco.....*Editor*  
 Howard Hassard .....*Executive Director*  
 Peart, Baraty & Hassard.....*Legal Counsel*

## House of Delegates

### TOTAL DELEGATES (329)

### DELEGATES EX-OFFICIO (69)

Ralph C. Teall, Sacramento.....President  
 James C. MacLaggan, San Diego.....President-Elect  
 William F. Quinn, Los Angeles.....Speaker of House of Delegates  
 Joseph W. Telford, San Diego.....Vice-Speaker of House of Delegates  
 Carl E. Anderson, Santa Rosa.....Chairman of Council  
 Matthew N. Hosmer, San Francisco.....Secretary  
 Dwight L. Wilbur, San Francisco.....Editor

#### COUNCILORS

Roger C. Isenhour (1967).....First District  
 Llewellyn E. Wilson (1967).....Office No. 1, Second District  
 Frank C. Melone (1968).....Office No. 2, Second District  
 Malcolm C. Todd (1968).....Office No. 1, Third District  
 Elmer F. Gooel (1966).....Office No. 2, Third District  
 Richard L. Taw (1967).....Office No. 3, Third District

Lewis T. Bullock (1968).....Office No. 4, Third District  
 Joseph P. O'Connor (1966).....Office No. 5, Third District  
 Franklin F. Ham (1967).....Office No. 6, Third District  
 Wilbur G. Rogers (1968).....Office No. 7, Third District  
 Joseph F. Maguire (1967).....Fourth District  
 Ralph W. Burnett (1966).....Fifth District  
 Richard S. Wilbur (1967).....Office No. 1, Sixth District  
 Albert G. Miller (1968).....Office No. 2, Sixth District  
 Malcolm S. M. Watts (1966).....Office No. 1, Seventh District  
 Roberta F. Fenlon (1967).....Office No. 2, Seventh District  
 Harold Kay (1966).....Office No. 1, Eighth District  
 William F. Kaiser (1967).....Office No. 2, Eighth District  
 Carl E. Anderson (1967).....Ninth District  
 James H. Yant (1968).....Tenth District  
 Forest J. Grunigen (1967).....Eleventh District  
 Edward B. Shaw (1966).....Scientific Board Representative

### ELECTED DELEGATES (269)

<i>Delegates</i>	<i>Alternates</i>	<i>Delegates</i>	<i>Alternates</i>
<b>ALAMEDA-CONTRA COSTA (19)</b>		<b>IMPERIAL (2)</b>	
Ackerman, Frederick	Adams, Robert	Jaquith, George	Ajalat, M. P.
Anderson, Conrad E.	Armstrong, James R.	Schoensee, Burke E.	Wilson, William C.
Bassett, J. Brandon	Barron, Gilbert		
Black, Daniel W.	Byers, Gilbert	<b>INYO-MONO (2)</b>	
Charvet, Leonard W.	Caldwell, Kendall W.	Hartwig, W. Ray	Alm, Theodore
Goetsch, Carl	Donald, William G., Jr.	Knecht, Evan	Denton, Robert W.
Goggio, Alfred	Duffy, Charles C.		
Hart, Charles J.	Eisenberg, Harold J.	<b>KERN (4)</b>	
Holden, Herbert	Etheredge, Samuel N.	Day, Robert L.	Anderson, Gene
Hoskins, H. Dean	Harms, Herbert	Osell, L. N.	Clark, M. Marlin
Hudson, Charles B.	Kirk, Ralph	Strongin, Seymour	Ellis, John F.
Keig, William	Lyman, Richard W.	Vaughan, J. E.	Friend, James R., Jr.
Kerns, Claude	Maloney, Harold		
Kunkel, Peter	Morrison, J. Evans	<b>KINGS (2)</b>	
Lewis, Gwilym B.	Purcell, Edward F.	Brookshier, R. W.	Christensen, L. F.
Richards, Dexter N., Jr.	Reedy, Richard N.	Kerr, Edwin E.	Dittes, William
Truman, Stanley R.	Rihn, Richard J.		
Twigg, Edward	Rosen, Edgar	<b>LASSEN-PLUMAS-MODOC-SIERRA (2)</b>	
Wiesinger, Warren E.	Ross, Joseph	Bross, Willard, Jr.	Batson, Wilbur C.
		Quinn, William J.	Davis, Fred J., Jr.
<b>BUTTE-GLENN (2)</b>			
Elmendorf, Thomas	Ritter, Dale W.	<b>LOS ANGELES (88)</b>	
Murphy, Franklin L.	Sears, A. R. M.	Allin, John G.	Anderson, James E.
		Andersen, George C.	Arcadi, John A.
<b>FORTY FIRST (3)</b>		Asher, Leonard M.	Austin, Robert Reed
<b>FRESNO (5)</b>		Attayah, Albert M.	Baker, Thomas
Argo, W. L.	Corbus, Howard	Axelrod, Bernard	Beattie, Arthur S.
Howard, Arthur F.	Frye, John	Bailey, Wilbur	Benson, Seymour
Kass, Robert	Gray, Clell C., Jr.	Baker, Jack W.	Berkaw, Kenneth
Smith, Robb	Swift, Coe T.	Barber, Clifford A.	Bleecker, Harry H., Jr.
Snyder, L. J.	Whitten, Richard	Barnes, Roger W.	Botzbach, Henry A.
		Barry, Donald J.	Brennan, John C.
<b>HUMBOLDT-DEL NORTE (2)</b>		Beason, Ralph D.	Brown, Albert F.
Loring, Theodore	Bux, Donald E.	Boyle, Joseph F.	Burch, John T.
Henderson, Justus	Smith, E. Kenneth	Buehler, George S.	Carlson, Carroll C.



## Delegates

Bullis, John A.  
 Bullock, Lewis T.  
 Burke, Donald E.  
 Burrows, Herbert L.  
 Campion, George M.  
 Case, Walter G.  
 Compton, Russell F.  
 Condit, Leonard O.  
 Conti, James G.  
 Crane, Jay J.  
 Crum, Jean F.  
 Doehring, Paul C.  
 Donahue, D. W.  
 D'Orazio, Edward  
 Dummer, Jerome  
 Ellison, G. Roger  
 Elshire, H. Donel  
 Fitch, Donald R.  
 Goldman, Theodore H.  
 Gondek, Frank R.  
 Goodwin, William E.  
 Goel, Elmer F.  
 Halasey, Thomas  
 Hamel, Neal C.  
 Hanchett, Richard B.  
 Haskell, M. M.  
 Heiser, Saul  
 Hill, Harry E.  
 Hoffman, Eugene F.  
 Hohl, Mason  
 Hood, Robert T., Jr.  
 Isaacs, Julien H.  
 Kiddie, Thomas  
 \*Kirchner, Arthur A.  
 Krantzdorf, Charles D.  
 Kuntz, George S.  
 Lau, Michael W.  
 Longmire, William P., Jr.  
 Ludwig, J. Lafe  
 Lynn, Jack M.  
 MacInnis, Douglas N.  
 Mailman, Richard H.  
 Mauer, Edgar F.  
 May, Lewis H. V.  
 Miller, Richard D.  
 Milliken, Ralph M.  
 Mooney, Herbert S.  
 Morgan, Henry G.  
 Morton, Daniel G.  
 Murrieta, A. J., Jr.  
 Neuenschwander, Robert S.  
 Ottalini, Guy Adams  
 Pheasant, Homer C.  
 Platz, Edward  
 Plechas, N. Peter  
 Pollack, John V.  
 Quinn, William F.  
 Rogers, Frank A.  
 Rothenberg, Sanford F.  
 Schimmel, Irwin  
 Shearer, Shirley K.  
 Smart, Reginald H.  
 Smith, Eldon E.  
 Smith, Thayer A.  
 Snell, Marvin V.  
 Stragnell, Robert  
 Taw, Richard L.  
 Voigt, Philip F.  
 Watson, Robert L., Jr.  
 Wiener, Thomas  
 Wilkins, Harold E.  
 Woodruff, John H.  
 Woolington, Sam S.  
 Yates, Paul D.  
 Zinn, Willard J.

## MARIN COUNTY (3)

Ablin, Arthur R.  
 Mills, Robert L.  
 Weden, Elmer, Jr.

## MENDOCINO-LAKE (2)

Roberson, B. B.  
 Smalley, Robert B.

## MERCED (2)

Jackson, Edward  
 McDowell, B. E.

## MONTEREY (3)

Fassett, James R.  
 Hull, Osman H.  
 Turner, Joseph E.

## NAPA (2)

Brignoli, Walter H.  
 Rose, Edgar Kash

## Alternates

Cheverton, William G.  
 Cooper, Boyd  
 Cope, Jerome A.  
 Dorn, Robert M.  
 Edwardes, Arthur F.  
 Edwards, Orville H.  
 Evans, Creed M.  
 Evashwick, George  
 Fields, Albert  
 Fisher, Neal R.  
 Ford, James H.  
 Fox, Saul L.  
 Frankfield, Robert H.  
 Freidin, Morris  
 Furer, Stanford A.  
 Golden, Robert F.  
 Golenternek, Joe  
 Harnagel, Edward E.  
 Herson, Ronald E.  
 Hoffman, Peter L.  
 Horton, James W.  
 Houts, Richard E.  
 Hull, Earl T., Jr.  
 Hull, Forrest E.  
 Jackson, Newton R.  
 Jennings, Elmer R.  
 Jones, Henry A.  
 Kawakami, Iwao G.  
 Kelso, Raymond, Jr.  
 Keltner, Mark R.  
 Lambert, Ross W.  
 Levy, Charles C.  
 Lopez, Henry L.  
 Marcus, Stanley  
 Mayne, John C.  
 Maytum, W. James  
 McCandless, Harrison  
 McLaughlin, Henry M.  
 Medler, David C.  
 Morgan, Frank M.  
 Mueller, Robert L.  
 Murray, Gregory C.  
 Nippell, Robert M.  
 Odou, Eugene R.  
 Oetting, Henry K.  
 Olch, David I.  
 Palmer, Robert H.  
 Parlour, Richard R.  
 Parris, Edward B.  
 Penka, Ernest J.  
 Peterson, John S.  
 Pocock, Dean S.  
 Rolland, Ward M.  
 Schade, Frank F.  
 Silver, Bernard B.  
 Smith, Seth W.  
 Stauffer, Floyd R.  
 Taylor, William A.  
 Thom, John G.  
 Turrill, Fred L.  
 Ulery, Richard M.  
 Vogel, Philip J.  
 Warren, Ward B.  
 Wasserman, John M.  
 Weber, Robert A.  
 Weiss, Benjamin J.  
 Westerbeck, Charles W.  
 Whipple, Winston F.  
 Wong, Thomas A.  
 Wood, Robert C.  
 Wunderlich, E. E.  
 Zimmerman, Norval F.

Alderson, Joseph J.  
 Lee, John R.  
 Wagner, Leo A.

Waring, William  
 Wilson, L. B.

Corbett, Thomas  
 Soderstrom, Edwin

Eldredge, Eugene E.  
 Kandlbinder, A. F.  
 Klinefelter, R. P.

Ashley, Robert C.  
 Ledwich, Thomas

## Delegates

### ORANGE (12)

Ball, Dexter T.  
 Carroll, Vincent P.  
 Eastman, Henry V.  
 Galbraith, Harold F.  
 Gerrie, Wallace A.  
 Graham, Ralph E.  
 Hawkins, G. William  
 Jett, Jim  
 Mosier, Laurance A.  
 Paul, Carl J.  
 Plumb, Hugh J., Jr.  
 Price, J. B.

### PLACER-NEVADA (2)

Dubin, Nathan  
 Joye, K. M.

### RIVERSIDE (4)

Abbott, Donald  
 Ivanoff, John C.  
 Jones, Cecil  
 Stone, H. H.

### SACRAMENTO (6)

Berg, John A.  
 Berman, A. E.  
 Farley, James O.  
 Grayson, Charles E.  
 Horn, Carl E.  
 Pope, Glenn A.

### SAN BENITO (2)

Haruff, John J.  
 Moore, Ernest

### SAN BERNARDINO (5)

Halburg, Clarence T.  
 Hendrickson, M. A.  
 Miano, Ben D. A.  
 Sprague, Charles P.  
 Varden, Arthur

### SAN DIEGO (13)

Carpenter, Walter F.  
 Fairchild, L. H.  
 Hippen, Robert L.  
 Hokr, William K.  
 King, Ralph M.  
 Levy, Edward I.  
 Messenger, Harold  
 Peck, Sam  
 Robinson, Frank H.  
 Rumsey, John M.  
 Tancredi, Chester  
 Telford, Joseph W.  
 Youel, Milo A.

### SAN FRANCISCO (19)

Bender, William T.  
 Biskind, Gerson R.  
 Combs, Robert C.  
 Fullenlove, Tom M.  
 Gallagher, Donald M.  
 Gibbons, Henry, III  
 Herrod, Chester E.  
 Herzog, George K., Jr.  
 Hopp, Eugene S.  
 O'Gara, Louis A.  
 Rixford, Emmet L.  
 Robinson, Saul J.  
 Saunders, John B. de C. M.  
 Schaupp, John B.  
 Sirbu, Abraham B.  
 Wayburn, Edgar  
 Webb, Eugene M.  
 Weyrauch, Helen B.  
 Williams, A. Justin

### SAN JOAQUIN (4)

Benn, James J.  
 Harrington, Donald C.  
 McNally, John  
 William, George

### SAN LUIS OBISPO (2)

Chambers, James R.  
 Kirk, Stanley

### SAN MATEO (7)

Brown, Henry A.  
 Fox, Norman C.  
 Hart, Ward L.  
 Hills, Oscar W.  
 Lindsey, Howard W.  
 Novak, Frank J.  
 Saidy, John T.

## Alternates

Fraide, Raul  
 Hastings, Charles M.  
 Kammerman, Richard F.  
 Kay, Fred M.  
 Martin, Walter H.  
 McFarland, Philip H.  
 Morgan, Russell M.  
 Nielsen, David I.  
 Schneider, Shirley M.  
 Siemonsma, Harry L.  
 Stonestreet, Marshall P.  
 Thompson, Arthur F.

Rossitto, T. J.  
 Shamhart, H. William

Kinney, William  
 Lyons, John C.  
 Stone, Vean M.  
 Zweig, Robert M.

Babbin, George  
 Cook, Orrin S.  
 Hause, Donald P.  
 Lambert, Lewis  
 Long, John B.  
 Martin, James W.

Currie, Norman L.  
 Jones, Peter

Gibson, Thomas  
 Hill, Harold M.  
 Krikes, Nicholas P.  
 Sterling, Allen F.  
 Wake, Donald K.

Brumbaugh, Simon C., Jr.  
 Corwin, Edward H.  
 Ford, John R.  
 Herrick, William C.  
 Kirtland, Howard B., Jr.  
 Moore, Stanley A.  
 Parkinson, Gaylord  
 Peabody, Homer D., Jr.  
 Pierangelo, Anthony J.  
 Plumb, Robert T.  
 Powell, E. R.  
 Tisdale, William  
 Wells, John J.

Auerback, Alfred  
 Baer, Charlotte C.  
 Baron, Shirley H.  
 Bonfilio, Nicholas D.  
 Bryan, John R.  
 Burnham, DeWitt K.  
 Clark, Albert G.  
 Cook, Robert E.  
 Erskine, John M.  
 Feldman, Sanford E.  
 Fleming, Ruth  
 Hurwitz, Samuel  
 Jacobs, Alvin H.  
 Kiyasu, William S.  
 Musser, Don C.  
 Pillsbury, Philip L.  
 Reinhardt, William O.  
 Salomon, Maurice S.  
 Webb, Gilbert A.

Evans, Wesley  
 Morozumi, John  
 Nickols, Bruce  
 Salter, Robert

Cletsoway, Richard W.  
 Greenman, Robert

Aycinena, Juan  
 Healy, Francis A.  
 Kohn, Martin M.  
 Larsen, William G.  
 Richanbach, Henry S.  
 Rossiter, Stanford B.  
 Storli, Edgar A.

\*Deceased.

<i>Delegates</i>	<i>Alternates</i>	<i>Delegates</i>	<i>Alternates</i>
<b>SANTA BARBARA (4)</b> Dalton, James McNiece, Kenneth Miles, Harold Ziemba, Joseph	Blanchard, John Domz, Casimir Gebhart, William Heiges, L. E.	<b>TULARE (2)</b> Goettle, James W. Lavers, George D.	Brauner, E. P. Wulff, Verna
<b>SANTA CLARA (12)</b> Besson, Gerald Boice, Clyde Clark, William H. Davis, Burt L. Foster, Thomas N. Fox, Leon P. Giansiracusa, Frank Liston, Edward Mitchell, Sidney Scarborough, C. Gerald Silver, Emmanuel Skillicorn, Stanley A.	Blanchard, Leland Cramer, Harold George, John W. Houck, George Hull, David I. Kaufman, S. Fred Manson, R. Morton Neubauer, Ivan O'Neill, Robert Peck, Clemmer Ramsay, George Rowles, Donald	<b>VENTURA (3)</b> Huff, W. Cloyce Moore, James W. Rulfo, Henry J.	Hair, Charles M. Hart, William L. Powell, Noble A., Jr.
<b>SANTA CRUZ (2)</b> DePuy, J. L. Rousseau, Robert	Mills, Richard Standage, Harlow	<b>YOLO (2)</b> Sobeck, Frederick J. Wilson, B. Kent	Edmondson, Robert C. Vaughn, T. Neil
<b>SHASTA-TRINITY (2)</b> Miller, Charles D. Polka, Michael G.	Gregory, Leonard Keye, John, Jr.	<b>YUBA-SUTTER-COLUSA (2)</b> Boyer, Warren Wright, Bayard A.	Cusick, George Wallace, Robert N.
<b>SISKIYOU (2)</b> Macfarlane, Robert Thompson, Victor	Chappell, Harry Schnack, William	<b>EX-OFFICIO SCIENTIFIC BOARD (18)</b> Belford, William W. Bettman, Jerome W. Biskind, Gerson R. Blanchard, Leland B. Brockman, Seymour J. Dillon, John B. Farber, Eugene M. Goerke, L. S. Grayson, Charles E. Kaufman, Joseph J. Keeney, Edmund L. Knox, Stuart C. Neufeld, Alonzo J. Petit, Donald W. Richards, Victor Rubin, David Russell, Keith P. Zaik, Edward J.	Kelly, Hobart M. Samson, Paul C. Stein, Justin J. Wood, David A.
<b>SOLANO (2)</b> Garrett, Robert L. Olson, William J.	Gullock, Alvin H. Schmutz, Melvin A.	<b>EX-OFFICIO PAST PRESIDENTS (22)</b> Peers, Robert A. .... 1935 Wilson, Harry H. .... 1940 Molony, Wm. R., Sr. .. 1942 Schaupp, Karl L., Sr. .. 1943 Goin, Lowell S. .... 1944 Cline, John W. .... 1947 Askey, E. Vincent .... 1948 Kneeshaw, R. Stanley 1949 Cass, Donald .... 1950 MacLean, H. Gordon ... 1951 Green, John W. .... 1953	Morrison, Arlo A. .... 1954 Shipman, Sidney J. .... 1955 Charnock, Donald A. .... 1956 MacDonald, Frank A. 1957 West, Francis E. .... 1958 Reynolds, T. Eric .... 1959 Foster, Paul D. .... 1960 Bostick, Warren L. .... 1961 Wheeler, Omer W. .... 1962 Sherman, Samuel R. .... 1963 Doyle, James C. .... 1964
<b>SONOMA (3)</b> Barnett, Richard C. Sharrocks, Horace F. Zieber, R. L.	Clary, David T. Craven, Wayne Johnston, Richard T.	<b>EX-OFFICIO HONORARY PAST PRESIDENT (1)</b> Murray, Dwight H.	
<b>STANISLAUS (3)</b> Nelson, William New, David J. Purvis, Robert	Goutiere, Vernon Hatch, F. N. Woolley, J. S.		
<b>TEHAMA (2)</b> Ingle, Gerald Wolfe, Lynn E.	Jourdan, Harve Wood, O. T.		

## CALPAC REPORTS

### Biltmore Bowl

Immediately Following the Opening  
Session of the CMA House of Delegates



# House of Delegates • 1966 Annual Session

## AGENDA

### Biltmore Bowl

*Speaker*.....William F. Quinn, Los Angeles  
*Vice-Speaker*.....Joseph W. Telford, San Diego  
*Secretary*.....Matthew N. Hosmer, San Francisco

FIRST MEETING, Saturday, March 19, 1966, at 7:00 p.m.

### ORDER OF BUSINESS

1. Call to order.
2. Report of Committee on Credentials, and Organization of the House of Delegates—Roll Call.
3. Announcement and approval of Reference Committees and Miscellaneous Announcements.
  - (a) Committee on Credentials. (Delegates must register with the Committee.)
  - (b) Reference Committee on the Reports of Officers, the Council, the Commissions and Standing and Special Committees (Reference Committee No. 1.)
  - (c) Reference Committee on Finance, to review the reports of the Secretary and the Executive Secretary and to study and make recommendations to the House of Delegates on the budget submitted by the Council and the amount of dues for the ensuing year. (Reference Committee No. 2.)
  - (d) Reference Committee on Resolutions and New and Miscellaneous Business. (Reference Committee No. 3.)
  - (e) Reference Committee (No. 3A) on Resolutions and New and Miscellaneous Business.
  - (f) Reference Committee on Amendments to the Constitution and Bylaws. (Reference Committee No. 4.)
  - (g) Reference Committee on CPS Business.
4. Address by President of the Woman's Auxiliary to the CMA—Mrs. George J. Bower.
5. Address by President—Ralph C. Teall.
6. Report of the President—Ralph C. Teall.
7. Report of the President-elect—James C. MacLaggan.
8. Report of the Speaker of the House of Delegates—William F. Quinn.
9. Report of the Vice-Speaker of the House of Delegates—Joseph W. Telford.
10. Report of the Trustees of the California Medical Association—Ralph C. Teall.
11. Report of Physicians' Benevolence Fund, Inc.—Ralph C. Teall.
12. Report of the Secretary—Matthew N. Hosmer.
13. Report of the Editor—Dwight L. Wilbur.
14. Report of the Executive Secretary.
15. Report of Legal Counsel—Peart, Baraty & Hassard.
16. Report of the Committee for Emergency Action—Ralph C. Teall.
17. Report of the Council—Carl E. Anderson, Chairman.
18. Report of CPS Board of Trustees—William H. Thompson, Chairman, Board of Trustees.
19. Reports of ad hoc committees of 1964 House of Delegates:
  - (a) Ad hoc Committee on 1965 Amendments to the Constitution and Bylaws—Robb Smith, Chairman.
  - (b) Ad hoc Committee on State Fee Schedules—Roger C. Isenhour, Chairman.
20. Reports of Commissions.
  - (a) Commission on Medical Services—Milo A. Youel, San Diego.
  - (b) Commission on Public Agencies—Albert G. Miller, San Mateo.
  - (c) Commission on Community Health Services—Harold Kay, Oakland.
  - (d) Commission on Communications—Malcolm C. Todd, Long Beach.
  - (e) Commission on Professional Welfare—George K. Herzog, Jr., San Francisco.
  - (f) Judicial Commission—Donald A. Charnock, Los Angeles.
  - (g) Commission on Allied Health Professions and Services—Forest J. Grunigen, Los Angeles.
  - (h) Commission on Hospital Affairs—Bert L. Halter, San Francisco.
  - (i) Scientific Board—Edward B. Shaw, San Francisco.
21. Reports of Other Committees.
  - (a) Bureau of Research and Planning—Samuel R. Sherman, San Francisco.
  - (b) Committee on Legislation—Dan O. Kilroy, Sacramento.
  - (c) Finance Committee—Harold Kay, Oakland.
  - (d) Medical Executives Conference—Mrs. Olive Neick, San Francisco.
  - (e) Delegates to the AMA—Burt L. Davis, Los Angeles.
22. Old and Unfinished Business.
23. New Business.

## SECOND MEETING, Tuesday, March 22, 1966, at 4:00 p.m.

(To be recessed and reconvened at 9:00 a.m. Wednesday, March 23)

### ORDER OF BUSINESS

1. Call to order.
  2. Supplemental report of Credentials Committee—Roll Call.
  3. Honored Guests.
    - (a) Fifty-year Members.
    - (b) Past Presidents.
    - (c) California Medical Assistants Association.
    - (d) California Nurses' Association.
  4. Introduction of President-elect of Woman's Auxiliary—Mrs. Samuel K. Bacon.
  5. Secretary's announcement of Council's selection of time and place for the 1967 Annual Session.
  6. Election of Officers:
    - (a) President-elect.
    - (b) Speaker.
    - (c) Vice-Speaker.
    - (d) Councilors (three-year terms except as noted).
      - (1) Third District—Office No. 2—Elmer F. Goel, Beverly Hills (term expiring).
      - (2) Third District—Office No. 5—Joseph P. O'Connor, Pasadena (term expiring).
      - (3) Third District—Office No. 8—Newly created office—term expiring 1969.  
*Third District—Los Angeles County.*
      - (4) Third District—Office No. 9—Newly created office—term expiring 1967.
      - (5) Fifth District—Ralph W. Burnett, Bakersfield (term expiring).  
*Fifth District—Calaveras, Fresno, Kern, Kings, Madera, Mariposa, Merced, San Joaquin, Stanislaus, Tulare and Tuolumne Counties*
      - (6) Seventh District—Office No. 1—Malcolm S. M. Watts, San Francisco (term expiring).  
*Seventh District—San Francisco County.*
      - (7) Eighth District—Office No. 1—Harold Kay, Oakland (term expiring).  
*Eighth District—Alameda and Contra Costa Counties.*
    - (e) Delegates to the American Medical Association: Delegates and Alternates to the American Medical Association are elected for terms of two calendar years. The Delegates and Alternates to be elected at this meeting will serve for two calendar years starting January 1, 1967, except as otherwise noted.  
  
INCUMBENTS:
      - (1) John G. Morrison, San Leandro (term expiring).
      - (2) \*Arthur A. Kirchner, Los Angeles (term expiring).
  - (3) Robert C. Combs, San Francisco (term expiring).
  - (4) J. Norman O'Neill, Los Angeles (term expiring).
  - (5) J. Lafe Ludwig, Los Angeles (term expiring).
  - (6) Burt L. Davis, Palo Alto (term expiring).
  - (7) Arlo A. Morrison, Ventura (term expiring).
  - (8) James E. Feldmayer, Exeter (term expiring).
  - (9) O. W. Wheeler, Riverside (term expiring).
  - (10) Malcolm C. Todd, Long Beach (term expiring).
  - (11) John E. Vaughan, Bakersfield (term expiring).
  - (f) Vacancy in Delegation due to death of Arthur A. Kirchner; one-year term commencing January 1, 1966.
  - (g) Alternates to the American Medical Association: Terms of all incumbents expiring. All offices for two-year terms starting January 1, 1967, except as otherwise noted.  
  
INCUMBENTS:
    - (1) Frederick Ackerman, Pleasant Hills (alternate to John G. Morrison).
    - (2) Dudley M. Cobb, Los Angeles (alternate to Arthur A. Kirchner).
    - (3) Emmett Rixford, San Francisco (alternate to Robert C. Combs).
    - (4) William F. Quinn, Los Angeles (alternate to J. Norman O'Neill).
    - (5) Harold Kay, Oakland (alternate to J. Lafe Ludwig).
    - (6) Leon P. Fox, San Jose (alternate to Burt L. Davis).
    - (7) Henry Brown, San Mateo (alternate to Arlo A. Morrison).
    - (8) Charles Grayson, Sacramento (alternate to James E. Feldmayer).
    - (9) Wilbur Bailey, Los Angeles (alternate to O. W. Wheeler).
    - (10) Alfred J. Murrieta, Jr., Los Angeles (alternate to Malcolm C. Todd).
    - (11) Joseph P. O'Connor, Pasadena (alternate to J. E. Vaughan).
7. Election of CPS Trustees (three-year terms):  
Reports of CMA Council as Nominating Committee.  
Incumbents, terms expiring:  
Mr. Ransom M. Cook, San Francisco.  
Carl E. Horn, Sacramento.  
Gregory C. Murray, Los Angeles.  
Herman H. Stone, Riverside (Ineligible for reelection).

\*Deceased.



William H. Thompson, San Mateo (Ineligible for reelection).

Stanley R. Truman, Oakland.

8. Announcements by Secretary.

Council's nominations of members of Commissions and Committees.

(For approval by the House of Delegates.)

9. Reports of Reference Committees:

(a) Reports of Reference Committee No. 1 on Reports of Officers, the Council, Commissions and Standing and Special Committees.

(b) Report of Reference Committee No. 2 on Reports of the Secretary, the Executive Secretary, and the budget and dues.

(c) Report of Reference Committee No. 3 on Resolutions and New and Miscellaneous Business.

(d) Report of Reference Committee No. 3A on Resolutions and New and Miscellaneous Business.

(e) Report of Reference Committee No. 4 on Amendments to the Constitution and Bylaws.

(f) Report of Reference Committee on CPS Business.

10. Unfinished Business.

11. New Business.

12. Presentation of Officers:

President—Presentation of plaque to President Ralph C. Teall.

President-elect.

Speaker.

Vice Speaker.

13. Approval of Minutes. (Committee to edit.)

14. Adjournment.

WILLIAM F. QUINN, *Speaker*

MATTHEW N. HOSMER, *Secretary*

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## 1965 CONSTITUTIONAL AMENDMENTS, FOR ACTION IN 1966

Under the terms of the Constitution, proposed constitutional amendments must lie on the table until the next regular meeting of the House of Delegates following the meeting at which they were introduced. A proposed amendment introduced at the 1965 meeting and to be acted upon in 1966 is presented below. In addition, one By-law amendment was introduced at the second session of the 1965 House of Delegates and, since it could not be acted upon for at least 24 hours, was held over for action in the next regular (1966) meeting.

The Proposed Constitutional amendment is required to be printed in two issues of the journal before it comes before the House of Delegates for action.

‘ ‘ ‘

### CONSTITUTIONAL AMENDMENT 1-65

Introduced by: The Council

Subject: Composition of Council

**Resolved:** That Article III, Part B, Section 9, paragraph (c) of the Constitution of the California Medical Association be amended by deleting the words "without the right to vote" at the end of the section, so that the section will read:

"(c) One (1) member of the Executive Com-

mittee of the Scientific Board to be elected by the Executive Committee of that body from representatives of the scientific sections or members-at-large."

‘ ‘ ‘

### BY-LAW AMENDMENT 22-65

Introduced by: Walter F. Carpenter

Representing: 1965 Reference Committee No. 2

Subject: Payment of Dues

**Resolved:** That Chapter 2, Section 10, Paragraph (b) of the Bylaws of the California Medical Association be amended by deleting the language shown below in parentheses and by adding the language shown below in italics, so that the section shall read:

"By Failure to Pay Dues. If the Annual assessments of dues, payable to this Association or the American Medical Association by any member of this Association, are not paid in full on or before (April) *March* 1, of any year, such member shall automatically lose his membership in this Association as of (April) *March* 1 of such year. The Council of this Association, in its discretion, upon payment of such unpaid dues, and any other assessments of dues accruing thereafter, may at any time reinstate such member."

# ANNUAL REPORTS FOR 1965

## Foreword

PRESENTED BELOW are the official reports of the governing bodies of the California Medical Association. These cover, for the most part, the calendar year 1965 and may be supplemented by additional reports to be made before the House of Delegates to cover activities occurring in the early part of 1966.

These reports will be reproduced in the *Annual Reports Bulletin* which will be distributed to all members of the House of Delegates in advance of the 1966 meeting of that body. This bulletin will also contain a number of reports from officers, commissions, bureaus and committees of the Association, which as a body will portray the entire picture of CMA activities during the year. Copies of this bulletin will be available to individual members requesting them following the Annual Session.

This procedure has been adopted as a means of informing the entire membership of the overall activities of the Association, of providing members of the House of Delegates with detailed reports on a number of areas of interest and of allowing the many officers, commissions, bureaus and committees to bring their reports more up-to-date for the consideration of the House of Delegates.

### REPORT OF

### *The Council*

*To the President and the House of Delegates:*

The Council of the California Medical Association has the dual responsibility of managing the daily affairs of the organization and determining policies to be followed between annual meetings of the House of Delegates. The variety and volume of business coming before the Council from these activities requires a tremendous amount of planning and organization as well as relatively frequent meetings.

The Council has followed a program of 10 meetings annually. This program has been maintained during the calendar year 1965. Three meetings have been scheduled for the early 1966 months preceding the Annual Session.

Minutes of all Council meetings are published in CALIFORNIA MEDICINE in the earliest issue available following each meeting. Many details of Council considerations and actions are contained in these reports. Additional details are also available from the Association's office and staff. Each member should feel free to request any desired information.

The composition of the Council is geographical, numerically uniform and representative of all major fields of practice of California physicians.

Council meetings are arranged so that reports may be made by all standing commissions and committees and by special committees appointed for specific purposes. Representatives of various allied interests are invited to attend and to participate. Their thoughts, ideas and suggestions are brought forth and considered. Ample opportunity is afforded all members and guests to speak freely and in detail. Officers of county medical societies are invited to attend each Council meeting. Council society executive secretaries attend regularly.

Councilor attendance at meetings is usually 100 per cent with an absence noted occasionally for good cause.

This report will not go into detail on Council actions but will discuss briefly some of the major areas of interest and

activities which have engaged the Council during the past year.

1. *Actions of the 1965 House of Delegates.* The Council supervised the implementation of all resolutions adopted by the 1965 House of Delegates. Copies of all resolutions adopted and a report on the actions taken have been mailed in advance of the 1966 House of Delegates meeting to all members of the House. Wherever feasible, the author of each resolution has been contacted and the actions on his resolution made known to him. Where resolutions have been introduced in the name of a delegation, the chairman of the delegation and/or the major county society within that delegation area has been informed and has been requested to notify the appropriate author.

2. *Liaison With Other Organizations.* The Council has maintained liaison with other organizations and with departments of the State government which are involved in medical programs and/or specific segments of the population. Numerous organizations and state agencies are invited to send a representative to each Council meeting and to present any information on the activities of their respective departments or agencies which seem appropriate and which is of interest to the medical profession. Among these organizations are California Physicians' Service, the California Hospital Association and the medical schools within the state. Among the departments of State government invited to all Council meetings and in regular attendance are the State Department of Public Health, Department of Social Welfare, Department of Mental Hygiene, Department of Rehabilitation and Department of Employment. The Council has been honored by frequent representations from the immediate past president of the State Board of Medical Examiners, Doctor Donald Abbott, and recently the new president, Doctor Nicholas Oddo. Mr. Paul Ward, director of the Health and Welfare Agency of the State, and Mrs. Lois Bower, president of the Woman's Auxiliary to the California Medical Association, have also been frequent guests of the Council. The Council has been impressed with the interest shown by these representatives in working with the



medical profession. These contacts serve to generate a personal relationship which is most helpful when Association policies must be expressed to the administrative branch of the State government and to other professional organizations or civic bodies.

It was the Council's pleasure to honor Doctor Malcolm H. Merrill, Director of the State Department of Public Health upon his retirement from that position. Doctor Merrill worked closely with the Association for 22 years. The Council voted unanimously to recommend to this meeting of the House of Delegates that Doctor Merrill be made an honorary member of the Association.

At the December meeting of the Council, it was our pleasure to welcome the new Director of the State Department of Public Health, Doctor Lester Breslow. It is our feeling that the long-standing spirit of mutual cooperation between the Department and the Association will be continued under the guidance of Doctor Breslow. We look forward to a long period of close relationship in the implementation of the many programs affecting medicine and public health.

The California Hospital Association has regularly sent one of its officers to each meeting of the Council and officers of this Association in turn have been invited to attend the meetings of the Board of Trustees of the CHA. This close rapport between the two organizations is unique and is most beneficial. We look forward to a continuation of this valuable working relationship.

Until recently, Mr. John Pompelli, Field Representative for the Division of Field Services of the AMA, attended Council meetings on a regular basis and kept us informed of AMA activities. Mr. Pompelli has been transferred to the Washington office of the AMA. Jerry Gould has assumed the responsibilities for the AMA field service in California. We welcome Mr. Gould and know that he will continue to represent the AMA in fine fashion.

3. *Legislation.* From a medical standpoint the 1965 general and special legislative sessions were the most important in California history. Many of the bills which were passed and subsequently signed into law by the Governor will have a far-reaching impact on physicians. Assembly Bill 5, the Casey Bill, as it was finally passed in a special session of the Legislature, is California's implementation of Title XIX of Public Law 89-97, the Federal Medicare program. This new California law tends to place the medically indigent and the needy in the mainstream of medical care. It will eventually bring about a conversion of county hospitals into community hospitals. Planning sessions are now underway to assure that the valuable teaching and training programs in county hospitals will not be adversely affected.

Other important legislation passed this year is contained in the so-called Stiern Bills on medical discipline—(Senate Bills Nos. 400-405). This legislation gives increased latitude of action to the State Board of Medical Examiners and establishes five regional committees or sub-boards. These committees, containing majority representation from county medical societies, will review formal complaints brought against physicians. It was heartening to learn that the State Board of Medical Examiners has requested the State Personnel Board to establish a special category of medically directed inspectors or field men to work within the areas of complaints resulting from the new areas of Board responsibility. The Council, acting through its ad hoc committee on medical discipline, served as a coordinating body for the recommendations from county medical societies and medical schools in compiling a list of nominees for appointment to these regional committees.

A close relationship exists with the State Board of Medical Examiners and the Council is looking forward to sharing with the Board the responsibility for maintaining high standards of professional conduct.

Another new law introduces major changes in the Workmen's Compensation System. It revamps the entire structure of the Industrial Accident Commission, changes the basis upon which schedules of minimum allowances are developed and the method by which independent medical examiners are selected. Another change provides the injured workman a more liberal second choice of physician. The Council's ad hoc Committee on Workman's Compensation made numerous presentations to legislative committees and has continued, since passage of the law, to work with the current chairman and Medical Director of the Industrial Accident Commission in the creation of the Industrial Medical Advisory Committee authorized for the first time in California. This new law became effective January 15, 1966.

In cooperation with compensation carriers, employers and other interested parties, a directory will be prepared by CMA listing all physicians in the state who are qualified and willing to treat injured workmen. Each practicing physician will have an opportunity to indicate his desire to be included in such a directory early in 1966.

Other legislative considerations, such as compulsory PKU testing and the establishment of two renal dialysis centers, demonstrate the increasing interest of the State Legislature in the manner of the provision of medical services.

The Council maintains close contact with its Legislative Committee. Through it the Association has been represented at all important hearings. The Council has interpreted policies of the Association to be followed on specific issues. The quality of medical representation in Sacramento continues on a high level.

Reports on legislative activities are made to the Council regularly and are conveyed to all members through regular communications channels, including *CMA News*, *CALIFORNIA MEDICINE* and the publications of the Public Health League of California. Many county society bulletins also publish digests of legislative proceedings so that their members may be kept advised.

The Council is grateful to the Public Health League for its continuing invaluable service to the profession.

In December 1964 the Association opened its Sacramento office, jointly established with the Public Health League. This office is maintained on a year-around basis and assists in maintaining necessary contacts with state officials, legislative and administrative bodies and other entities. This office has already proved to be of major importance in assisting the officers and staff of the association.

On the national scene, your Council and officers have been much involved in Public Law 89-97 (Medicare) and Public Law 89-239 (Regional Programs on Heart Disease, Cancer and Stroke). The Council has established task forces on each of these new federal laws. The Task Force on P.L. 89-97 has been hard at work in informing physicians of California regarding the implications of this program. The Task Force, chaired by President Ralph C. Teall, has performed a yeoman task in working with CPS and other interested organizations, and in dealing with the difficult problems of certification of facilities, utilization review plans and prevailing, usual and customary fees.

The Council, by unanimous vote, requested California Physicians' Service to attempt to qualify and be designated as a carrier for Part B of Title XVIII of P.L. 89-97.

California is privileged to have a number of men serving



on advisory committees to the Social Security Administration, and also to have Roberta Fenlon, M.D., a member of the Council, serving on a temporary basis as a special medical consultant to Mr. Arthur Hess, Director, Bureau of Health Insurance of the Social Security Administration.

With respect to P.L. 89-239, the Council Task Force, chaired by the President-Elect, James C. MacLaggan, M.D., has been concerned with the effects of this law, a result of the DeBaKey Commission report, on medical practices in California. The CMA is fortunate in having three representatives on a California Coordinating Council for Implementation of P.L. 89-239. This Council, composed of representatives of medical and hospital associations, medical schools, the State Health Department and other groups, is attempting to coordinate planning grant applications made possible by P.L. 89-239.

4. *Commission and Committee Activities.* All commissions and committees submit their own reports to the House of Delegates in the Annual Reports Bulletin. They also report to the Council regularly. The Council's actions based on these reports appear in the published Council minutes. The Commissions established by the Association are extremely busy and perform a valuable service to the Council and the entire Association in carrying out their respective assignments. Your Council cannot compliment too highly the many individual physicians serving on the Commissions and Committees of the Association for their contributions to medicine in California and nationally.

It is with great pride that the Council observes the evolving maturity of the Scientific Board. The Board is continuing to follow the concepts set forth in the "Wilbur Report" and is making giant strides toward strengthening and coordinating the scientific activities of the Association.

The Commission on Communications continues to make a most valuable contribution to the Association. Extreme demands have been placed on the Communications staff during this past year, and both the Commission and the staff have performed admirably under very demanding circumstances. Communications both within and outside the Association are of such vital importance that a well-rounded, seasoned yet imaginative department is vital to the continuing strength and stature of the Association.

The Council continues to view with pride the activities of the Bureau of Research and Planning. The Research Department functioning for the California Medical Education and Research Foundation as well as the Bureau of Research and Planning, works closely with all other committees and carries the responsibility for research activities of the Association.

The newly-formed Commission on Hospital Affairs has been deeply involved in continuing medical staff surveys and in voluntary health facility planning. The importance of both of these activities in the coming years cannot be over-emphasized.

The future of medicine in California and the role CMA should play in it, received attention and in-depth consideration by the Council at a special meeting in October. The attitudes developed at this special meeting could have far-reaching effects on CMA's future.

In keeping with the powers delegated to it by the House of Delegates and the Constitution and Bylaws of the Association, the Council evaluated the purposes and policies of CMA, its staff and financial structure, measuring those against the task medicine will face in the next several years. Each member of the House of Delegates has received a summary of the discussions held at that very important meeting. For the benefit of the membership as a whole, that summary is repeated here. Following are some of the observations, attitudes and actions of the Council:

#### A.—OBSERVATIONS

1. CMA has maintained a healthy *balance* between the activities of its physician-members (voluntary) and its executive staff (salaried).

2. CMA's *financial* reserves have fallen considerably below the commonly accepted yardstick of "one year's income." This has been due to increasing membership without the concomitant increases in financial reserves.

3. The *enormous impact* of recent and proposed medical care legislation, both Federal and State, will require much greater involvement on the part of CMA. This will almost certainly cause an increase in voluntary physician-committee activities and salaried staff to serve them.

4. *Administrative expenses* have decreased in the past five years when measured as a percentage of total expenditures. *Scientific, educational and membership services* have increased if the same yardstick is used.

5. The *staff* has achieved a high degree of efficiency as a result of *fluidity* and *flexibility* in the shifting of work assignments.

#### B.—ATTITUDES

Attitudes which represent a consensus of Council opinions:

1. There should be a more clearly defined organizational division of CMA to conduct liaison and advisory activities to governmental administrative agencies at all levels. CMA committees and staff should be augmented, as necessary, for this purpose.

2. Effective communications is a vital necessity. Some activities to promote improved communications might include:

a. Greater involvement of CMA delegates and alternates as channels of communications to the membership.

b. Research and evaluation of communication activities to increase their effectiveness.

c. Increased use of CMA field staff to work with component societies and other groups.

d. Coordination of communication activity with legislative and governmental relations efforts to strengthen medicine's influence in this field.

e. Possible expansion of CMA offices (which are now located in Sacramento, Los Angeles and San Francisco).

3. There should be a continuing review of CMA committee activities to avoid overlapping and duplication of functions. Some fluidity must be maintained because of rapidly changing developments on the state and national levels.

4. An increase in CMA dues will probably be required to support increased involvement in guiding governmental proposals in the medical care field, to increase communications efforts and to re-establish the level of financial reserves. An alternative to the latter might be a reduction in the dues allocation now given to AMA-ERF. The Finance Committee now plans to study these alternatives.

#### C.—SPECIFIC COUNCIL ACTIONS

1. After reviewing the 1958 Council action regarding the position of Executive Director, the Council reaffirmed its previous action and voted to continue the position with its designated staff responsibilities. (Mr. Howard Hassard continues to serve the Association as Executive Director.)

2. The Executive Director is to confer with CMA officers, management consultants and others for the purpose of presenting plans to the Council to implement many of the attitudes and observations outlined in the foregoing paragraphs.

3. Each CMA Councilor is encouraged to develop communications efforts in his own district—involving CMA delegates to the extent possible—particularly with reference to the implications of current national and state laws and proposed legislation.

The ability of medicine to guide government and the public toward decisions which are consistent with sound medical practices depends on strong medical leadership, supported by the informed advice and opinions of practicing physicians in every part of California. Your views and recommendations will be welcomed by each of the CMA Officers and your District Councilor.

The Council will present a supplemental report to the House of Delegates indicating actions taken pursuant to this special meeting.

*Conclusions:* The above digest represents only the high spots of the Council's concerns and activities during 1965.



Many additional items can be found in a review of the minutes of the 1965 meetings, but those presented are singled out as representative of some of the major areas of interest in the past year. The Council is deeply indebted to the President and President-Elect, both of whom have been more than willing to devote their time, efforts and talents to the complex responsibilities of representing the CMA before any number of private and public bodies. Both Doctor Ralph C. Teall and Doctor James C. MacLagan have been unstinting in their service and to each we all owe a debt of gratitude. The same applies to a number of Councilors, commission and committee members, AMA delegates and others who have given so freely of their time and talents in presenting the true picture of medical practice in California. Special thanks are also due our dedicated staff of loyal employees who must and do adjust to the demands of the moment. Without their devoted service, the work of the Association could not be accomplished.

The Council wishes to call your attention to the report of the Executive Secretary, especially the concluding paragraph.

Respectfully submitted,

CARL E. ANDERSON, M.D., *Chairman*

#### REPORT OF THE

### *Committee for Emergency Action*

*To the House of Delegates:*

The Committee for Emergency Action was formed several years ago to provide a small body of responsible officers who could meet for decisive action at times when the Council of the California Medical Association was not in session. Such actions are subject to approval by the Council.

During the past year, the Committee has functioned in this capacity and has held several meetings and telephone conferences on matters requiring immediate action and not deferrable to the next Council meeting. Its decisions have always been referred to the Council at its next meeting and have consistently been approved by that body. A report of the Committee's activities is a regular part of the Council's agenda and is made a part of the Council minutes which are regularly published in CALIFORNIA MEDICINE.

This Committee is composed of the President, the President-Elect, the Speaker of the House of Delegates and the Council Chairman. It is my opinion that this Committee serves an essential purpose and is responsive to the wishes of the Council as its governing body.

Respectfully submitted,

RALPH C. TEALL, *Chairman*

#### REPORT OF

### *Trustees of the California Medical Association*

*To the House of Delegates:*

Trustees of the California Medical Association is a non-profit corporation organized for the express purpose of holding excess funds of the California Medical Association. Its members are at all times the members of the Council of the Association.

The corporation holds an annual membership meeting at the time of the organization meeting of the Council, immediately following the adjournment of the House of Delegates, and meets on the call of the president when business must be transacted. Daily affairs are handled by the staff of the Association.

Principal holdings of the corporation at this time are Government bonds representing the investment of accumulated funds, the 693 Sutter building which houses the Association's offices and several trust funds for the benefit of employees and affiliates. These are listed on the financial report appearing on another page of this issue. Members are urged to review the financial report so that they may become familiar with the reserves behind the Association.

Respectfully submitted,

RALPH C. TEALL, *President*

#### REPORT OF THE

### *Delegation to the AMA*

*To the President and the House of Delegates:*

Although the nature of the delegation's activities are generally known to many of the physicians of California, not too many of our members are fully aware of the considerable amount of planning and detail, as well as the number of meetings and special activities, which are held before, during, and after each of the two conventions which take place each year. This progress report will therefore describe briefly some of these elements, as well as some of the more tangible results of the delegation's work during the past year.

Before doing so, however, I should like to express my sincere appreciation and that of the delegation to Doctor J. Lafe Ludwig who has recently completed his term as Chairman of the delegation, and under whose aegis the delegation has been reorganized to function more effectively and efficiently in carrying out its duties and responsibilities on behalf of the California Medical Association.

Prior to each AMA convention the members of each of the standing committees of the delegation, of which there are six in number, confer to make plans for the duties they will assume while they are attending the conventions. The six committees are Rules, Resolutions, Hospitality, Candidates, Ace-Deuce, and Alternates. Each of these committees has a specific set of responsibilities and, at the various caucuses of the delegation which occur every day, the Chairman of each committee reports on matters and subjects of interest and on which decisions must be made by the delegation. Whether the decisions affect the rules under which the delegation operates, or the attitudes of the delegation with regard to resolutions submitted by other delegations, or how to argue for and urge the adoption of resolutions which arise out of actions of this House of Delegates or from county medical societies, or the assignments made to members in staffing the hospitality suite, or what arrangements are made to sponsor various candidates for vacancies on numerous AMA committees, or what assignments are made in developing and promoting relationships with smaller states or with delegates and alternate delegates of other delegations—are all matters which occupy the attention of the entire delegation. The six standing committees therefore perform a very active role in involvements of all types, and each member, whether an alternate or delegate, has specific responsibilities assigned to him, following which he reports to the members of his committee or to the entire delegation at the appropriate time.



An important activity of the entire delegation is that of meeting on the occasion of the CMA House of Delegates in order to discuss various matters in advance of the following AMA meeting. Another activity is to meet with the Council prior to attending each AMA convention. It is at this time that various policy positions are hammered out and courses of action are determined.

The delegation maintains a record of the various topic and reference committee preferences of each delegate and alternate so that, as resolutions are assigned to the AMA Reference Committees, interested and knowledgeable delegates may have an opportunity to participate in the Reference Committee hearings and to voice opinions and to support the actions of the California Delegation and of the CMA House of Delegates. A record is also maintained of the contacts between members of the CMA delegation and delegates from other states so that each member can perform his duties most effectively.

As previously indicated, the delegation caucuses at breakfast and again at lunch every day during the AMA convention; it meets as often as necessary at other times on immediate call of the Chairman whenever developments necessitate such meeting—and this is a very common occurrence. Following each AMA convention the Chairman of the delegation presents a report to the Council on the delegation's activities and the major happenings and actions at the AMA conventions. It is a distinct pleasure to report that the California delegation has, in the majority of instances, been successful in securing the adoption of resolutions it has submitted and has been instrumental in many situations in shaping AMA policy. Where the delegation has been unsuccessful on occasions, it has attempted to pursue its objectives at subsequent conventions or through contact with various Councils and Committees of the AMA in order to secure further consideration of its point of view.

It is important to note that there is no unit rule that binds the delegation to any one single opinion or to the selection or sponsorship of any single candidate regardless of the position which he seeks. All points of view are encouraged and each member of the delegation may voice his opinion based upon his judgment of the particular situation or the specific candidate.

To provide the delegates with some idea of the volume of problems and issues with which the CMA delegates had to concern themselves at the recent Clinical Convention of the AMA, I need only mention that there were 65 resolutions presented as well as 15 supplementary reports to the Board of Trustees and 17 supplementary reports of the Councils and Committees of the AMA. These, of course, were in addition to the annual reports published by the numerous councils and committees which had to be read and digested in advance of the convention. Some of the actions of the AMA House at the Clinical Convention which received considerable publicity and which should be mentioned for their importance are as follows: approval of the Board of Trustees' recommendation to increase AMA dues effective January 1, 1967, from \$45 to \$70. This matter will come up again at the annual convention and will be voted upon again at that time, inasmuch as the action will require a bylaw change which must lay over for one year. A number of resolutions dealt with P.L. 89-97 and matters such as constitutionality of the legislation, billing practices, and fees. The recommendations of the Gunderson Committee Report on the reorganization of the House of Delegates were reviewed and acted upon, with a considerable number not approved. One of those approved concerned itself with the size of the AMA House; when its membership reaches 250 delegates representation will be on the basis of 1/1,250 members rather than the present ratio of 1/1,000 members. At the present time the

size of the House is 236 in number. Several resolutions as well as a report of the Board of Trustees concerned themselves with the formation of a planning and development section, or with an institute to study the role of medicine in society. The Board of Trustees was authorized to set up a study committee which will report to the AMA House at the annual convention to be held in Chicago.

The foregoing represent just a handful of the actions taken, but are indicative of the wide scope of problems which present themselves for deliberation, discussion and action.

As newly elected Chairman it is my hope to improve communications between your delegation to the AMA with all physicians in component societies and to acquaint our House of Delegates with various problems facing your delegation. This closer liaison will enable us to serve you all the more effectively and to promote the points of view and the policy actions which this House espouses.

Respectfully submitted,

BURT L. DAVIS, *Chairman*

#### REPORT OF THE

### *Physicians' Benevolence Fund, Inc.*

#### *To the House of Delegates:*

Physicians' Benevolence Fund, Inc., continued its benevolent activities during 1965 in the same manner as in previous years. It continued making monthly contributions to Los Angeles County Physicians Aid and responded to calls for temporary assistance from physicians or their families throughout the state.

The fund received \$28,910 in income in the fiscal year ended June 30, 1965 and made expenditures of \$15,340 during that period. The excess of \$13,570 of income over expenditures went directly into reserves. Total assets now stand at \$179,022. Income was derived from \$21,181 contributed by the California Medical Association at the rate of \$1 from the dues of each active member, \$3,586 contributed by the Woman's Auxiliary and \$4,143 received in interest from investments and loans to affiliated organizations.

During the fall months the Operating Committee of the fund met to review both activities and policies. Without going into detail it is well to repeat here that contributions by the fund are based on immediate need and are not designed to constitute a retirement income program, that all appeals are investigated at the local level, that periodic reports on recipients are furnished and that all cases of real need are handled sympathetically and tactfully. The recipients generally are widows and children of physicians.

An Operating Committee composed of Clyde L. Boice, chairman, and Doctors Elizabeth Mason Hohl, Dudley M. Cobb, Jr., Alexander Fraser, Don C. Musser and George Wolf has been continually interested and active in guiding the policies of this fund and our thanks go to them for their dedicated services. There are no paid employees of the fund and the only operating expenses are the cost of an annual audit and the cost of an occasional meeting of the Operating Committee.

Thanks are also due the Woman's Auxiliary to the California Medical Association, which has continued its activities to raise funds for this activity and to make most generous contributions for its operations.

Respectfully submitted,

RALPH C. TEALL, *President*



## Executive Secretary

### *To the President and the House of Delegates:*

This report is made in behalf of the entire staff of the California Medical Association and will be concerning itself with the broad aspects of Association activities and status. Further details will be made available on request to the Reference Committee of the House of Delegates or to any member. The period covered by the report will be essentially the calendar year 1965.

1. *General.* The Association maintains its principal office and records at 693 Sutter Street, San Francisco, a building owned by the Trustees of the California Medical Association, an affiliated corporation whose members are at all times the members of the CMA Council. While several tenants are housed in the building, the Association occupies about three-quarters of all usable space. The need for additional space is pressing and we are now working with an architect in a space and realignment study for the entire building.

The Los Angeles office has one executive employee and one secretary. The Sacramento office, opened in 1964 as a joint effort with the Public Health League of California, has provided needed space to serve as headquarters for the Legislative Committee and legislative activities during legislative sessions and is available the year round for committee members and others whose assignments take them to the state capital. Members of other professional groups comprising the Public Health League of California also find the new office a convenience throughout the year.

Membership in the California Medical Association has continued to increase and each month sees a new high point in total membership. As pointed out in this report in each of the past several years, increased membership brings with it increased demands for service. Added services and projects mean added personnel and increased expense. Some limited new activities can be taken on by the present staff and facilities while others require additional office space, executive and clerical expense, and travel and meeting costs necessarily determined by the nature of the project undertaken.

2. *Personnel.* At the end of 1965 the Association had 60 full-time employees on the payroll, two more than a year earlier. Several changes were made during the year in work assignments and others are being contemplated to meet the needs of our expanded activities in the area of government relations and communications.

Each year a review is made of the entire payroll for clerical and secretarial employees and an adjustment made, if necessary, to bring salaries in line with leading employers. Today the Association is rated, for payroll levels, among the average of employers in the region and, in addition, presents to employees such fringe benefits as group life insurance, retirement annuity, and travel insurance which are considerably higher than average. These benefits are made available as a means of making employment attractive and decreasing employee turnover.

3. *Financial.* The handling of finances running into millions is a constant assignment to the staff and includes the management of the Association itself and four subsidiary organizations: Trustees of the California Medical Association, Physicians' Benevolence Fund, Inc., Six Ninety Three Sutter Publications, Inc., and California Medical Education and Research Foundation.

Annual financial reports of all these organizations appear on another page of this issue in the form of balance sheets

and operating statements for the fiscal years ended June 30, 1965. These figures are taken directly from the reports of John F. Forbes and Company, certified public accountants.

For the California Medical Association the annual report shows that a net gain of \$33,103 of income over expenditures was registered for the fiscal year, compared with a net gain of \$220,893 for the preceding fiscal year.

The report shows total income from members' dues of \$1,442,953, an increase of 2.55 per cent from dues income of \$1,407,017 for the preceding fiscal year.

Administrative expenses for the past year totaled \$523,395, an increase of 27.6 per cent over the \$410,145 recorded for the earlier year. Expenditures for scientific, educational and communications activities totaled \$898,468, or 14.2 per cent higher than the \$786,973 expended in the 1964 fiscal year. On a comparative basis, the costs were somewhat higher in 1965 than in the preceding year.

Decreased advertising revenues again marked the fiscal year for CALIFORNIA MEDICINE, which received \$186,135 from advertising compared with \$205,867 in 1963. Despite this, revenue did increase in 1965, 8.68 per cent above the 1964 level of \$171,273. Publishing costs continue to increase yearly. In 1964, these costs increased 5.7 per cent above the 1963 costs. In 1965, publication costs rose from the earlier year level of \$244,542 to \$267,685, an increase of 9.45 per cent. Net results, after the application of \$3 per active member as income to the journal, showed a net loss of \$11,513 compared with a net loss of \$5,700 a year earlier.

The financial report of Trustees of the California Medical Association, which is actually a holding company for accumulated net assets of the Association, shows that the year ended with a net gain of \$32,944 of income over expenditures, compared with a net gain of \$36,731 for the 1964 fiscal year. The headquarters building, owned by the Trustees, showed a net gain of \$15,728 for the year, against a net gain of \$19,440 a year earlier.

For the 1966-67 fiscal year the staff has been working with the Finance Committee of the Council in preparing a budget which will finance the projected activities of the Association. The proposed budget approved by the Finance Committee of the Council will be given to the Council for approval and then will go to the 1966 House of Delegates, which must give final approval. Several policy matters will be referred to the House for decision as well.

During the closing months of each calendar year, the Association has, for several years past, been forced to borrow funds to meet its obligations during the year-end and the early months of the next year. These borrowings, requiring interest payments, have been necessitated in great part by the custom of some component societies which collect CMA and AMA dues from their members and do not forward these dues to the CMA until just before the April 1 deadline date. This procedure forces a large volume of work on the CMA at one time and results in delayed recognition of their payments by the individual members. While there has been some improvement in this condition, certain component societies followed this practice again in 1965 and required the Association to resort again to bank borrowing. While the component societies may find that investing these funds for a short period of time may bring in some interest income, it is obvious that the overall financial situation of the CMA is being handicapped and that prompt forwarding of dues when collected will do much to insure an orderly and prompt handling of membership details and will save the Association the necessity of paying interest on borrowed funds and eliminate peak work loads.



4. *Membership.* On September 1, 1965, the date on which an official membership count is taken for purposes of representation in the House of Delegates, the Association showed 21,358 active members, a gain of 564 over the total recorded a year earlier. Membership gains were reported by 34 component societies, while three showed a membership loss and three showed no change. The sizable gains were a result of the transfer of former members of the Forty First Society as well as new members.

On the basis of active memberships all Councilor Districts will retain their present representation on the Council, except District III, which is now entitled to two additional Councilors, one with an initial term of three years and the other with an initial term of one year.

The active membership of all component societies as of September 1, 1965, and the same date a year earlier is shown in the following table:

Active Membership in the CMA by Component Societies

<i>Societies</i>	<i>Sept. 1, 1965</i>	<i>Sept. 1, 1964</i>
Alameda-Contra Costa .....	1,752	1,653
Butte-Glenn .....	106	96
Forty First .....	225	1,867
Fresno .....	371	324
Humboldt-Del Norte .....	93	87
Imperial .....	48	46
Inyo-Mono .....	15	11
Kern .....	258	255
Kings .....	37	34
Lassen-Plumas-Modoc-Sierra .....	24	27
Los Angeles .....	8,695	7,478
Marin .....	242	234
Mendocino-Lake .....	60	60
Merced .....	72	62
Monterey .....	210	198
Napa .....	88	84
Orange .....	1,072	854
Placer-Nevada .....	89	70
Riverside .....	324	292
Sacramento .....	540	520
San Benito .....	9	9
San Bernardino .....	442	388
San Diego .....	1,165	1,051
San Francisco .....	1,819	1,806
San Joaquin .....	270	237
San Luis Obispo .....	92	87
San Mateo .....	579	564
Santa Barbara .....	323	303
Santa Clara .....	1,145	1,035
Santa Cruz .....	128	124
Shasta-Trinity .....	77	78
Siskiyou .....	25	23
Solano .....	89	73
Sonoma .....	205	191
Stanislaus .....	183	169
Tehama .....	17	17
Tulare .....	122	110
Ventura .....	215	159
Yolo .....	61	57
Yuba-Sutter-Colusa .....	71	61
TOTAL .....	21,358	20,794

5. *CALIFORNIA MEDICINE.* The journal continued its program of improved quality during 1965 and remains as one of the preeminent state medical journals in the country. A better grade of paper for improved portrayal of illustrations and x-rays and a new type face for the editorial pages for improved readability have increased costs, while at the same time, improving the readability and overall quality of the journal.

Financially the journal went backward somewhat in the fiscal year ended June 30, 1965. Its total income increased from \$171,273 to \$186,135, an increase of 8.68 per cent. In the same period the cost of production rose 9.46 per cent. Net result for the year showed an excess of expense over income of \$11,513 after taking into account the sum of \$3 per dues-paying active member as income. For the preceding fiscal year the net loss on this basis was \$5,700.

The decline in advertising income resulted from curtailment by many pharmaceutical producers of their journal advertising, a trend which has held for several years. Present requirements of the U.S. Food and Drug Administration are held accountable for this trend and are continuing to hold many former advertisers out of the market. Prospects for 1966 are more promising but it is still too early to make any firm predictions.

The Advertising Manager for CALIFORNIA MEDICINE now represents the medical associations of the eleven western states and their respective journals. This pooled approach to advertising sales promises to contribute either to the revenues of all represented journals or to a reduction in costs.

6. *Annual Session.* Plans are well under way at the close of 1965 for the 1966 Annual Session. This will be held in Los Angeles, which housed the 1964 meeting. The usual problems of space and arrangement of meetings to make efficient use of available rooms prevail again but will be worked out in the best possible fashion before the start of the meeting. Annual meeting arrangements require the combined and cooperative efforts of the staff, the scientific sections and officers and the Woman's Auxiliary. All, fortunately, give their complete cooperation in the effort to produce as fine a meeting as possible with the material and space available. Advance appearances for 1966 indicate that a highly successful and efficient operation will be produced and that members may count upon the full attention of the staff in seeing to their comfort and convenience.

For the scientific program, the Scientific Board has assured the Council that an even more outstanding program will be presented, complete with scientific exhibits, medical motion pictures, closed circuit television and technical exhibits. The interest of specialty organizations is becoming evident in annual session planning and the coming meeting gives assurance that many topics heretofore presented only to specialty groups will be presented at a large CMA meeting. Both general and specialized topics will be available to the anticipated large registration.

Your attention is called to the numerous conferences scheduled throughout the meeting. We hope that this type of program addition and planning will supplement the scientific program with a resultant overall increase in physician attendance.

7. *Conclusion.* As 1965 closes it is well to remind the membership again that the CMA staff is here to be of service. Ideally the staff must be of a size which can assimilate new activities and programs and handle them with skill. At the same time, there is no room for an inefficient organization set up to handle peak loads of activity and remain virtually unemployed during slack periods. Your staff today appears to be of a size where new programs cannot be undertaken without personnel additions. Flexibility is and will be maintained and is today apparent in the staff organization.

In return, the thanks of the staff are extended to the officers, members of the Council and the numerous commission and committee chairmen and members who devote their own time and talents to the many problems facing a large organization. Without the devotion of these many members to their assignments and responsibilities the work of the California Medical Association could not go forward so smoothly. The staff as a whole is deeply appreciative of the leadership provided by these officials.

John Hunton, deeply respected friend of physicians throughout the United States, died December 2 at his home in San Francisco from a massive coronary attack.



The above report was prepared by Mr. Hunton and is presented to the membership in original form.

On October 1, 1965, John Hunton completed 25 years of service to medicine as the Association's Executive Secretary. At its October 30th meeting, the Council was privileged to honor him for his many contributions and outstanding leadership.

The CMA has been honored by his service and contributions.

Respectfully submitted,

HOWARD HASSARD, *Executive Director*

MATTHEW N. HOSMER, *Secretary*

#### REPORT OF

### *California Physicians' Service*

*To the President and the House of Delegates:*

**Membership.** As of December 1, 1965, the membership of California Physicians' Service-Blue Shield totaled 1,151,005 persons, representing a net gain of 28,000 persons over the corresponding date in 1964. Physician Membership on December 1, 1965, was 17,381, an increase of 597 for the 12-month period.

**Financial.** Based on actual experience for the first 11 months, plus estimated figures for December, CPS operating income for the calendar year 1965 from CPS commercial and government programs was approximately \$110,000,000. Operating income from the commercial programs totaled more than \$72,000,000 while \$38 million was handled under the government-financed programs which CPS serves as fiscal administrator.

Disbursements for medical and hospital services under the CPS commercial plans and the government programs totaled more than \$103 million during 1965, an increase of some \$13 million over 1964.

On December 1, 1965 the stabilization reserve fund stood at approximately \$18,700,000. This figure is equivalent to about three months' claims costs, and therefore conforms to the reserve formula recommended by the National Association of Insurance Commissioners for Blue Shield and Blue Cross plans.

**Research and Experimentation.** The experimental work with payment of "usual, customary, and reasonable" fees, begun by CPS in 1959, which culminated in offering "usual fee" programs in the statewide group market during 1964-1965, has been providential in view of the enactment of the Social Security Medicare legislation (PL 89-97) which embodies the principle of payment for professional services on the basis of "reasonable" charges. The experience, statistical guides, and county society liaison relating to the payment of usual, customary, and reasonable fees which CPS has accumulated and developed during the past seven years should place both California medicine and CPS in a favorable position with respect to Medicare coverage. Whether or not CPS is designated as a Medicare carrier, it has already provided CMA with valuable assistance in planning for Medicare, and will be able to assist further in the future.

Past experimentation with benefits for psychiatric care has also proven useful in view of the new out-patient psychiatric benefits to be provided through CPS-Blue Shield to members of the United Auto Workers union in California. Although this union has previously provided some inpatient psychiatric coverage for its members through contracts negotiated with management, the outpatient benefits are a new step and will involve about 25,000 employees, plus some 50,000 dependents in California.

The value of research and experimentation has been demonstrated repeatedly and effectively. CPS-Blue Shield continues, as it has in the past, to push its research and field testing along a broad front, including the areas of progressive patient hospital care, home nursing, outpatient consultative care, infant coverage, and others indicated by new developments in the patterns of medical practice. Frequently such efforts are long-term but their ultimate value can be suggested by a quote from a recent letter to CPS from the Executive Editor of *Medical Economics*: "I am impressed with how far ahead you are compared with the rest of the country."

**Fee Schedules.** The progressive updating and upgrading of fee schedules has resulted in an almost complete redistribution of the membership, with respect to applicable fee schedules, during the past few years. Ten years ago only the "A" and "B" schedules, which have now disappeared almost entirely, were available. Ninety-eight per cent of the membership held the "A" schedule, with its composite unit value of \$2.92, and the balance of 2 per cent held the "B" schedule, with its composite unit value of \$3.67. In 1959 when the first schedule based on the California Medical Association Relative Value Studies became available to CPS, a progressive program of fee schedule upgrading was established. Early in 1966, approximately 90 per cent of the CPS membership will hold programs including fee schedules with RVS unit values of \$5 or more. Due to the long time period during which CPS had no new schedules to effect an orderly transition to higher fees, the redistribution of fee schedules has not been accomplished without pain. Resistance to the higher costs required to support higher fee schedules has resulted in sales resistance and also in excessively high cancellation, both of which seriously hampered the numerical growth of the membership. Nevertheless, the updating policy was followed persistently on the valid premise that economically obsolete fee schedules, while they can be sold at lower rates, clearly are contrary to the facts of the economy and are, in fact, inequitable to the consumers as well as the providers of medical services. It is gratifying to report that at the present time the best informed buyers of health coverages increasingly agree with this view. Further, the activities in the past have now placed CPS in a position where it should not find itself again in a situation where a sizable portion of the membership is enrolled under programs with fee schedules which have fallen out of date.

The CPS Extended Service Program, combining the "usual fee" and fee schedule concepts, will get its biggest and most important test beginning January 1, 1966. On that date the Extended Service Program will become effective under a joint Blue Shield-Blue Cross program for employees of the State of California. Approximately 86,000 persons, including employees and dependents, will be covered under this new joint plan which has been established to replace CPS programs previously available to State employees. The Extended Service Program is designed to pay "usual, customary, and reasonable" fees to CPS Physician Members for covered services rendered to employees whose family income is \$7,500 annually or more. Payments for employees whose family income is \$7,500 or less, will be based on the 1964 RVS with a unit value of \$5.00 (CPS Schedule 4D). Payments to non-member physicians, regardless of the employee's income, will be based upon Schedule 4D.

**Public Assistance Medical Care and MAA Programs.** According to preliminary year-end figures, Public Assistance Medical Care and Medical Assistance for the Aged Programs administered by CPS disbursed \$31,800,000 in 1965 for medical care, a rise of 29 per cent over 1964. Of

the total, more than \$14 million was disbursed under MAA, the balance representing payments made under the PAMC outpatient program. These programs will be phased out beginning March 1, 1966 with the implementation of the new "Casey Bill" (AB 5).

*Casey Bill (AB 5) and "Medicare" (PL 89-97).* Assembly Bill 5, known as the "Casey Bill" after its author, Assemblyman Jack T. Casey of Bakersfield, was enacted during the 1965 special session of the California Legislature and signed in November 1965 by Governor Brown. It is now a State statute and beginning in March will be the basis for all State-financed medical programs for those eligible for State aid. The Federal Social Security "Medicare" program enacted by the Congress during 1965 also will soon go into effect, with benefit payments scheduled for July 1966.

The new State and Federal legislation presents a great opportunity, and a great challenge, to CPS and other qualified medical service plans and to their professional and hospital sponsors as well. Both the opportunity and the challenge of the legislation lie in the implicit presumption that private professional and administrative enterprise can achieve the objectives of providing the highest quality of medical services at a cost consistent with the best interests of all concerned—including those of the taxpayers.

It is understood that both the "Casey Bill" and the Social Security "Medicare" program will provide for payment of professional services on the basis of "usual, customary and reasonable" charges. This is a most important forward step in government financed programs.

CPS again is fortunate in having behind it the experience provided by the Santa Barbara County prepaid welfare recipient medical program, as well as considerable experience with "usual and customary" fee plans. This background will prove invaluable if CPS is selected to serve the programs established under AB 5 and PL 89-97.

*Military Dependents Program.* During the calendar year 1965, 75,000 claims for medical services rendered military dependents were processed by California Physicians' Service. Payment in the amount of \$5,618,590 was made to physicians.

Although the number of claims received during 1965 was less than that of 1964, the claims received increased during the last quarter. This was due to the increase of military strength in Vietnam. Dependents of service personnel who are sent overseas have a choice of military or civilian medical care without the approval of a military base, and the use of civilian medical facilities by these dependents increased.

California continues to process in excess of 20 per cent of all claims under this program in the United States.

*California Physicians' Insurance Corporation.* CPIC, the indemnity insurance company of which CPS owns all outstanding stock, attained a gross annualized premium income of \$5,460,300, as of September 30, 1965, up from \$3,400,000 as of September 30, 1964. Marketing only group indemnity surgical-medical-hospital coverages, group major medical benefits, and group life policies, CPIC's admitted assets on September 30, 1965 totaled \$2,010,137, as compared with assets of \$1,724,505 on September 30, 1964. These figures are exclusive of furniture, fixtures and reserves for depreciation.

*National Blue Shield.* Programs embodying the usual fee concept recently have assumed greater importance at national level as well as locally. During 1964, responding to market demands for broad professional benefits at predictable costs, National Association of Blue Shield Plans developed a form of "usual and customary fee plan," which was titled the Prevailing Fees Program.

This new program, the subject of intense study and development for more than a year, had gone into effect in five states and was approved for use in about two dozen others before the end of 1965. The Council of the CMA accepted a recommendation of the CMA Liaison Committee to CPS for the CMA Committee on Fees and the Bureau of Research and Planning to cooperate with CPS in pilot studies to determine the feasibility of such programs here in California. At year's end, preparations for these pilot studies were under way.

Accounts written on a national basis make up an important segment of CPS membership, and include such groups as the Federal Employees program and the various United Auto Workers groups. The UAW groups and the Federal Employees plan as well include professional benefits based on the Relative Value Studies at a \$5 unit value. National Blue Shield is currently negotiating with the United States Steel and its unions for a program which would be a "usual fee" plan here in California.

Respectfully submitted,

WILLIAM H. THOMPSON, M.D.  
*President and Chairman of the Board  
California Physicians' Service*

#### REPORT OF THE

### *Finance Committee*

*To the President and the House of Delegates:*

The Finance Committee presents at this time the complete financial reports of the California Medical Association and its affiliated organizations, all for the fiscal year ended June 30, 1965. These are taken directly from the audits made by John F. Forbes and Company, certified public accountants, and appear on another page in this issue of the *Journal*.

During the year this Committee has various obligations, including the preparation of an annual budget and the consideration of methods to be used in raising funds for projects which have not been foreseen during the budget preparation period or which are approved by the Council for action.

Committee meetings are held as frequently as needed, so that each item presented by the Council is acted upon promptly. Meetings on the 1966-67 budget have been held since October and will continue until a budget is agreed upon for referral to the Council and the House of Delegates.

Respectfully submitted,

HAROLD KAY, *Chairman*



**CALIFORNIA  
MEDICAL  
ASSOCIATION**  
(A Nonprofit Organization)

ASSETS	
CASH .....	\$ 92,562
CERTIFICATE OF DEPOSIT—CROCKER-CITIZENS NATIONAL BANK .....	800,000
ACCOUNTS RECEIVABLE, NET .....	79,485
NOTES RECEIVABLE—CENTRAL CALIFORNIA BLOOD BANK .....	\$ 84,500
Less reserve .....	84,500
NOTE RECEIVABLE—TRUSTEES OF THE CALIFORNIA MEDICAL ASSOCIATION....	30,000
FURNITURE AND FIXTURES (at nominal value) .....	1
ACCRUED INTEREST .....	6,050
PREPAID EXPENSE AND DEFERRED CHARGES:	
Insurance .....	\$ 1,590
Retirement program premium .....	16,431
Deposits .....	1,410
Other .....	2,532
TOTAL .....	<u>\$1,030,091</u>

Balance Sheet  
June 30, 1965

EXHIBIT A

LIABILITIES	
ACCOUNTS PAYABLE:	
American Medical Education Foundation .....	\$203,655
Other .....	130,775
LOAN PAYABLE—PHYSICIANS' BENEVOLENCE FUND, INC. ....	70,000
DEFERRED INCOME:	
Dues and subscriptions applicable to the period	
July 1 to December 31, 1965 .....	\$654,579
Other .....	1,101
EXCESS OF LIABILITIES OVER ASSETS (DEFICIT) (Exhibit B) .....	(30,019)
TOTAL .....	<u>\$1,030,091</u>

See notes to financial statements

	YEAR ENDED JUNE 30	
	1965	1964
INCOME:		
Dues and general:		
Membership dues less portion allocated		
to "CALIFORNIA MEDICINE" subscription .....	\$1,442,953	\$1,407,017
Fee for collection of American Medical		
Association dues .....	9,347	9,111
Interest earned .....	13,541	7,290
Other .....	638	293
Total .....	<u>\$1,466,479</u>	<u>\$1,423,711</u>
Official journal "CALIFORNIA MEDICINE":		
Advertising .....	\$ 186,135	\$ 171,273
Nonmember subscriptions .....	2,793	2,472
Reprints, net .....	1,945	1,215
Total .....	<u>\$ 190,873</u>	<u>\$ 174,960</u>
Less expenditures .....	<u>267,685</u>	<u>244,542</u>
Net (cost) .....	<u>\$ (76,812)</u>	<u>\$ (69,582)</u>
Allocated portion of members' dues .....	65,299	63,882
Net excess (deficiency) after allocation .....	<u>\$ (11,513)</u>	<u>\$ (5,700)</u>
TOTAL .....	<u>\$1,454,966</u>	<u>\$1,418,011</u>
EXPENSES:		
Administration .....	\$ 523,395	\$ 410,145
Scientific, educational, and communications .....	898,468	786,973
TOTAL .....	<u>\$1,421,863</u>	<u>\$1,197,118</u>
EXCESS OF INCOME OVER EXPENSES FOR THE YEAR .....	<u>\$ 33,103</u>	<u>\$ 220,893</u>
OTHER CREDITS (CHARGES):		
Reduction in reserves on account of payment on loans	\$ 8,000	\$ 5,500
Expenses applicable to prior years .....		(4,997)
TOTAL .....	<u>\$ 8,000</u>	<u>\$ 503</u>
EXCESS OF ASSETS OVER LIABILITIES:		
Increase for the year .....	\$ 41,103	\$ 221,396
At beginning of year (deficit) .....	(71,122)	(292,518)
AT END OF YEAR (Note 2) (deficit) .....	<u>\$ (30,019)</u>	<u>\$ (71,122)</u>

See notes to financial statements

Statement of Income  
and Expenses  
for the  
Years Ended  
June 30, 1965 and 1964

EXHIBIT B

**CALIFORNIA  
MEDICAL  
ASSOCIATION**

**Statement of  
Administration Expenses  
for the  
Years Ended  
June 30, 1965 and 1964**

**EXHIBIT B—SCHEDULE 1**

		YEAR ENDED JUNE 30	
		1965	1964
<b>SALARIES (see note) :</b>			
Executive .....	\$ 56,998	\$ 56,175	
Other .....	78,233	69,174	
Total .....	\$135,231	\$125,349	
<b>OFFICE:</b>			
Rent .....	\$ 17,692	\$ 16,012	
Supplies .....	24,587	18,305	
Equipment purchases and maintenance .....	7,560	6,703	
Telephone and telegraph .....	16,139	13,262	
Postage .....	5,621	2,600	
Professional fees (other than legal) .....	3,130	5,130	
Los Angeles office (other than salaries) .....	4,451	3,852	
Sundry .....	4,517	3,946	
Total .....	\$ 83,697	\$ 69,810	
Less services charged to other accounts (including billings to others of \$14,916 and \$12,989) .....	\$ 39,984	\$ 38,233	
Net .....	\$ 43,713	\$ 31,577	
<b>LEGAL .....</b>	<b>\$ 40,728</b>	<b>\$ 36,529</b>	
<b>MEETINGS:</b>			
Annual session .....	\$ 51,016	\$ 39,344	
American Medical Association .....	65,693	26,811	
Student-American Medical Association .....	5,414	4,797	
Council .....	11,152	11,030	
Medical Society executives .....	7,829	8,795	
County officers' conference .....	8,139	7,890	
Total .....	\$149,243	\$ 98,667	
Less annual session exhibitors' fees .....	39,245	40,260	
Net .....	\$109,998	\$ 58,407	
<b>TRAVEL:</b>			
Council .....	\$ 30,047	\$ 25,639	
Officers .....	25,575	16,954	
Administrative .....	16,002	13,889	
Total .....	\$ 71,624	\$ 56,482	
<b>GROUP INSURANCE AND RETIREMENT PROGRAM:</b>			
Retirement Program—Current service .....	\$ 27,543	\$ 23,577	
Retirement Program—Past service .....	6,313		
Group Life Insurance .....	9,842	8,549	
California Physicians' Service .....	15,527	14,328	
Total .....	\$ 59,225	\$ 46,454	
<b>OTHER:</b>			
The Woman's Auxiliary .....	\$ 7,971	\$ 7,772	
Physicians' Placement Service .....	21,450	16,908	
Payroll taxes .....	19,438	16,695	
Personal property taxes .....	2,566	2,140	
Dues and subscriptions .....	6,239	4,790	
Insurance .....	3,682	4,008	
Interest .....	1,050	2,554	
Sundry .....	480	480	
Total .....	\$ 62,876	\$ 55,347	
<b>TOTAL .....</b>	<b>\$523,395</b>	<b>\$410,145</b>	

NOTE: The total payroll for years ended June 30 was \$497,609 for 1965 and \$444,935 for 1964, of which \$362,378 and \$319,586, respectively, are included in other expense classifications or were charged to other organizations.



YEAR ENDED JUNE 30

SCIENTIFIC, EDUCATIONAL, AND COMMUNICATIONS:

	1965	1964
Medical services .....	\$ 42,203	\$ 30,596
Public agencies (Note 1) .....	39,103	27,172
Community health services .....	60,591	52,158
Bureau on communications .....	213,844	183,743
Scientific board .....	62,217	60,936
Medical education (Note 2) .....	18,696	18,628
Cancer committee .....	10,144	17,060
Professional welfare .....	30,015	28,212
Bureau of research and planning .....	76,753	75,127
Committee on legislation .....	77,828	48,243
Special committees of the council .....	33,848	17,288
Contributions:		
American Medical Education Foundation .....	201,000	195,958
Physicians' Benevolence Fund, Inc. ....	21,181	20,682
California League for Nursing .....	3,000	3,000
California Commission for the Accreditation of Nursing Homes and Related Facilities .....	2,750	3,000
Medical Libraries .....	5,295	5,170
TOTAL .....	\$898,468	\$786,973

OFFICIAL JOURNAL "CALIFORNIA MEDICINE":

Printing .....	\$176,127	\$160,010
Salaries .....	41,257	37,890
Advertising sales expenses:		
Salary .....	16,508	15,550
Travel .....	8,532	6,841
Sundry .....	1,281	2,581
Rent .....	3,516	3,516
Telephone and telegraph .....	3,729	3,475
Postage and mailing .....	10,480	9,800
Addressograph and supplies .....	2,675	2,430
Illustrations .....	2,852	2,916
Editorial .....	2,325	600
Discounts .....	3,271	2,896
Bad debts .....		1,025
Sundry .....	2,332	1,612
Total .....	\$274,885	\$251,142
Less representation fee .....	7,200	6,600
NET .....	\$267,685	\$244,542

NOTE 1: In 1965, the amount shown is after State participation of \$4,015.

NOTE 2: Medical education expenses are reflected net of the following credits:

	1965	1964
Postgraduate fees .....	\$14,553	\$16,827
Special grants applied .....	3,027	6,234
TOTAL .....	\$17,580	\$23,061

NOTE 1: The California Medical Association, in addition to the Group Pension Program effective January 1, 1961, has made provision for a Past Service Pension for certain full time employees. The unpaid balance due on the single premium required to fund this Past Service Pension at June 30, 1965, aggregated \$23,097. This amount, to be paid out of future operations, has not been set up as a liability on the books of the Association at June 30, 1965, and is not reflected in the accompanying financial statements.

NOTE 2: The California Medical Association is one of the defendants in an action in the San Francisco Superior Court in which damages of \$6,200,000 are sought. In the opinion of Counsel, the liability to the California Medical Association will consist only of the costs of defense, which are not presently ascertainable.

NOTE 3: The California Medical Association has agreed to indemnify the California Physicians' Service for losses incurred in the payment of benefits under the MD-Plan 65 Contract (1959) in excess of 90 per cent of the dues income collected. According to information furnished by the California Physicians' Service it is not expected that any liability will accrue to California Medical Association.

NOTE 4: The California Medical Association and the California Osteopathic Association have jointly agreed that the California College of Medicine (formerly College of Osteopathic Physicians and Surgeons) shall receive funds of at least \$225,000 per year for a period of four years from 1962. It is the opinion of the management, that the California Medical Association will not be called upon for any funds in addition to those already provided.

Statement of  
Expenses other than  
Administrative  
for the  
Years Ended  
June 30, 1965 and 1964

EXHIBIT B—SCHEDULE 2

Notes to  
Financial Statements  
June 30, 1965

**TRUSTEES OF THE  
CALIFORNIA MEDICAL  
ASSOCIATION**

(A Nonprofit Organization)

**Balance Sheet  
June 30, 1965**

**EXHIBIT A**

ASSETS	
CASH .....	\$ 29,521
UNITED STATES TREASURY BONDS, AT MATURITY VALUE (market value, \$1,021,331) (Note 4) .....	1,121,000
NOTE AND ACCOUNT RECEIVABLE .....	2,633
ACCRUED INTEREST ON BONDS .....	1,536
INVESTMENTS, AT COST:	
Pacific Magnetic Tape Equipment Co. (Note 1) .....	\$ 9,000
Six Ninety Three Sutter Publications, Inc. ....	1,000
PROPERTY, AT COST (subject to mortgage) :	
Land .....	\$ 87,400
Building and improvements .....	295,938
Total .....	\$383,338
Less accumulated depreciation .....	59,749
Net depreciated value .....	323,589
EQUIPMENT, AT NOMINAL VALUE .....	1
CASH SURRENDER VALUE OF LIFE INSURANCE POLICY .....	30,780
PREPAID INSURANCE .....	375
REAL ESTATE TAXES APPLICABLE TO SUBSEQUENT YEAR (contra) .....	10,500
TOTAL .....	<u>\$1,529,935</u>

LIABILITIES	
CALIFORNIA MEDICAL ASSOCIATION:	
Note payable .....	\$ 30,000
Account payable .....	2,507
MORTGAGE PAYABLE .....	63,728
OTHER ACCOUNTS PAYABLE AND ACCRUED INTEREST .....	246
ACCRUED REAL ESTATE TAXES (contra) .....	10,500
TRUST FUNDS .....	97,741
DEFERRED COMPENSATION PAYABLE .....	10,500
EXCESS OF ASSETS OVER LIABILITIES:	
Contributed .....	\$883,193
Excess of income over expenses (Exhibit B) .....	431,520
TOTAL .....	<u>1,314,713</u>
	<u>\$1,529,935</u>

See notes to financial statements

**Statement of Income  
and Expenses  
for the Year Ended  
June 30, 1965**

**EXHIBIT B**

INCOME:	
Excess of property income over expenses (Schedule 1) .....	\$ 15,728
Other:	
Interest on United States Treasury bonds and bills .....	\$28,772
Dividend (Pacific Magnetic Tape Equipment Co.) .....	900
Miscellaneous .....	53
Total income .....	<u>29,725</u>
	\$ 45,453
EXPENSES (other than property) :	
Fees .....	\$ 1,961
Insurance .....	197
Total expenses .....	<u>2,158</u>
Remainder .....	\$ 43,295
OTHER CHARGES:	
Net premium on life and retirement insurance policy .....	\$ 4,351
Provision for the retirement or other benefit of an employee of an affiliated organization .....	3,000
Provision for deferred compensation .....	3,000
	<u>10,351</u>
EXCESS OF INCOME OVER EXPENSES:	
Current year .....	\$ 32,944
Beginning of year .....	398,576
END OF YEAR .....	<u>\$431,520</u>

See notes to financial statements



# INCOME FROM RENTALS:

California Medical Association .....	\$52,332
Others .....	19,226
<b>TOTAL .....</b>	<b>\$71,558</b>

## TRUSTEES OF THE CALIFORNIA MEDICAL ASSOCIATION

# EXPENSES:

Utilities .....	\$ 4,838
Janitor service and maintenance .....	15,012
Repairs—Plumbing, electric, etc. ....	4,097
Alterations .....	3,645
Insurance .....	854
Elevator inspection and service .....	1,376
Supplies .....	694
Sundry .....	221
<b>Total .....</b>	<b>\$30,737</b>
Taxes .....	10,172
Interest on mortgage .....	2,873
Interest on borrowed money for purchase of property and making improvements thereon .....	1,980
<b>Total before depreciation .....</b>	<b>\$45,762</b>
Depreciation .....	10,068
<b>TOTAL .....</b>	<b>55,830</b>

EXCESS OF PROPERTY INCOME OVER EXPENSES ..... \$15,728

## Statement of Property Income and Expenses for the Year Ended June 30, 1965

EXHIBIT B—SCHEDULE 1

NOTE 1: The Trustees of the California Medical Association, as a nonprofit corporation, owns all of the outstanding stock of the Pacific Magnetic Tape Equipment Co., which was formed for the purpose of merchandising magnetic tape equipment as an adjunct to the activities of the Audio-Digest Foundation, a wholly-owned subsidiary of the California Medical Association. An unaudited financial statement of the Pacific Magnetic Tape Equipment Co., as of June 27, 1965, reflects a net worth of \$22,898 at that date, which is not shown on the books of the Trustees.

## Notes to Financial Statements June 30, 1965

NOTE 2: The portion of the Trust Funds applicable to the retirement or similar benefit to Mr. and Mrs. Ben H. Read, amounting to \$51,000 at June 30, 1965, has not been segregated from other assets of the corporation as directed by Chapter XVII of the bylaws of the corporation which states: "... All assets of this fund shall be held separate and apart from all other assets and property of the corporation ..."

NOTE 3: The Trustees of the California Medical Association is guarantor to the Crocker-Citizens National Bank for loans to a maximum amount of \$46,000 for the California Commission for Accreditation of Nursing Homes and Related Facilities. Loans outstanding under this guaranty at June 30, 1965 were reported to aggregate \$46,000.

NOTE 4: The United States Treasury bonds, kept in a custodian account with the Crocker-Citizens National Bank, are pledged to that bank for loans when and if needed, and for loans for which the Trustees are guarantor. There were no direct loans payable at June 30, 1965.

**PHYSICIANS'  
BENEVOLENCE FUND, INC.**  
(A Nonprofit Organization)

**Statement of Assets  
June 30, 1965**

**EXHIBIT A**

ASSETS		
CASH—CROCKER-CITIZENS NATIONAL BANK .....		\$ 9,007
INVESTMENTS:		
U.S. Treasury 2½% bonds at maturity values:		
Due December 15, 1969 .....	\$10,000	
Due December 15, 1972 .....	34,000	
Total investments (market value, \$40,234) .....		44,000
NOTE RECEIVABLE SECURED BY DEED OF TRUST—LOS ANGELES COUNTY PHYSICIANS AID ASSOCIATION (original amount, \$50,000—due in quarterly installments of \$1,000 plus interest at 2½% per annum) .....		
		34,000
DUE FROM CALIFORNIA MEDICAL ASSOCIATION:		
Note receivable .....	\$70,000	
Contributions receivable .....	20,848	
Accrued interest on note at 3% per annum .....	1,050	91,898
OTHER ACCRUED INTEREST RECEIVABLE .....		117
TOTAL .....		<u>\$179,022</u>

**SOURCE OF ASSETS**

CONTRIBUTED AT ORGANIZATION .....	\$ 92,132
EXCESS OF INCOME OVER EXPENDITURES (Exhibit B) .....	86,890
TOTAL .....	<u>\$179,022</u>

**Statement of Income  
and Expenditures  
for the Year Ended  
June 30, 1965**

**EXHIBIT B**

INCOME:		
Contributions:		
California Medical Association (see note) .....	\$21,181	
The Woman's Auxiliary of the California Medical Association .....	3,586	\$24,767
Interest earned:		
U.S. Treasury bonds and bills .....	\$ 2,189	
Loans .....	1,954	4,143
TOTAL .....		<u>\$28,910</u>
EXPENDITURES:		
Payments to beneficiaries:		
Los Angeles County Physicians Aid Association .....	\$ 6,000	
Others .....	8,750	
	\$14,750	
Other .....	590	
TOTAL .....		<u>\$15,340</u>
EXCESS OF INCOME OVER EXPENDITURES:		
Current year .....		\$13,570
Beginning of year .....		73,320
END OF YEAR .....		<u>\$86,890</u>

NOTE: The constitution of the California Medical Association, Article IV, Section 6, provides: "At least \$1 out of the annual dues paid by each active member of the Association shall be allocated to the Physicians' Benevolence Fund, Inc., a corporation, and shall be used for the purposes as set forth in that corporation's Articles and Bylaws."



ASSETS	
CASH IN BANK .....	\$69,537
LIABILITIES AND (DEFICIT)	
PAYABLES:	
Due to California Medical Association .....	\$16,703
Other .....	167
Total .....	\$16,870
UNEXPENDED PORTION OF GRANTS RECEIVED:	
United States Department of Health, Education, and Welfare (Note 1) .....	\$ 3,231
State of California Department of Mental Hygiene .....	12,426
Total .....	15,657
UNEXPENDED PORTION OF RESTRICTED CONTRIBUTIONS RECEIVED .....	38,750
EXCESS OF INCOME OVER EXPENDITURES (DEFICIT) .....	(1,740)
TOTAL .....	\$69,537

See notes to financial statements

**CALIFORNIA MEDICAL  
EDUCATION AND  
RESEARCH FOUNDATION**  
(A Nonprofit Organization)

Balance Sheet  
June 30, 1965

EXHIBIT A

	Total	Audio- Digest Foundation	U.S. Dep't. of Health, Education, and Welfare	Dep't. of Mental Hygiene State of California	California Medical Association	General Funds
INCOME:						
Grants and restricted contributions .....	\$63,199	\$25,000	\$ 5,000	\$33,199		
Other .....	3,534				\$3,534	
TOTAL .....	\$66,733	\$25,000	\$ 5,000	\$33,199	\$3,534	
EXPENDITURES:						
Contribution—California College of Medicine .....	\$25,000	\$25,000				
Services:						
Administrative .....	22,051		\$ 9,879	\$12,172		
Other .....	7,140		2,516	4,624		
Consultants and authors .....	2,250			2,250		
Supplies and printing .....	3,088		553	290	\$1,980	\$ 265
Key punch processing .....	377		377			
Mailing and postage .....	473		325	41	72	35
Telephone and telegraph .....	69		36	4	25	4
Travel and meeting .....	2,088		421	229	1,438	
Charge to cover payroll taxes and employee benefits .....	2,118		974	1,144		
Professional fees .....	525					525
Other .....	38			19	19	
TOTAL .....	\$65,217	\$25,000	\$15,081	\$20,773	\$3,534	\$ 829
UNEXPENDED PORTIONS OF GRANTS ON RESTRICTED CONTRIBUTIONS RECEIVED:						
Increase (decrease), current year .....			\$(10,081)	\$12,426		
Balance, June 30, 1964 .....	\$38,750		13,312			
Balance, June 30, 1965 .....	\$38,750		\$ 3,231	\$12,426		
EXCESS OF INCOME OVER EXPENDITURES (DEFICIT):						
Increase (decrease), current year .....						\$ (829)
Balance, June 30, 1964 .....						(911)
Balance, June 30, 1965 .....						\$(1,740)

See notes to financial statements

Statement of  
Income  
Expenditures  
and  
Fund Balances  
for the  
Year ended  
June 30, 1965

EXHIBIT B

NOTE 1: The Foundation has been awarded community health project grants by the United States Department of Health, Education, and Welfare, which has been applied as follows:

Period of Grant	Amount of Grant†	Funds Received	Expenditures Applied	Unused Balance
6-1-62- 5-31-63 .....	\$14,700	\$11,777	\$ 8,182	\$3,595*
6-1-63- 5-31-64 .....	26,131	14,132	13,606	4,121*
6-2-64-11-30-65 .....	43,113	15,778	16,668	3,231
		\$41,687	\$38,456	\$3,231

\*Applied to succeeding grant.

NOTE 2: The Foundation received a contract in the amount of \$44,265 from the California State Department of Mental Hygiene for the study of means of meeting the shortage of mental health personnel in California. At June 30, 1965, the Foundation had received \$33,199 against which expenditures of \$20,773 were charged. An additional sum of \$7,378 was received in July, 1965 for May and June installments.

Notes to  
Financial  
Statements  
June 30, 1965

**SIX NINETY THREE  
SUTTER  
PUBLICATIONS, INC.**

Balance Sheet  
June 30, 1965

**EXHIBIT A**

ASSETS	
CASH .....	\$17,287
ACCOUNTS RECEIVABLE .....	804
INVENTORY .....	15,097
DEPOSIT AND DEFERRED ORGANIZATIONAL EXPENSE .....	75
<b>TOTAL .....</b>	<b>\$33,263</b>

**LIABILITIES AND STOCKHOLDER'S EQUITY**

**LIABILITIES:**

Accounts payable .....	\$ 768
Account payable California Medical Association .....	22,715
Federal income tax payable .....	1,548

Total liabilities ..... \$25,031

**STOCKHOLDER'S EQUITY:**

Capital stock (authorized, 2,500 shares of \$10.00 par value each; issued and outstanding, 100 shares) (see note) .....	\$ 1,000
Retained earnings (Exhibit B) .....	7,232

Total stockholder's equity ..... 8,232

**TOTAL .....** **\$33,263**

**NOTE:** The Trustees of the California Medical Association are the sole stockholder of this Corporation.

**Statement of Income  
and Retained Earnings  
for the Year Ended  
June 30, 1965**

**EXHIBIT B**

**OPERATING REVENUE:**

Sales .....	\$29,649
Cost of goods sold .....	17,068

**GROSS PROFIT ON SALES .....** **\$12,581**

**EXPENSES:**

<b>Office expense:</b>	
Services .....	\$1,800
Rent .....	300
Supplies .....	879
Fees .....	375
Other .....	27
	<b>\$ 3,381</b>

<b>Shipping expense:</b>	
Services .....	\$ 498
Postage, freight, and express, net .....	731
	<b>1,229</b>

Personal property taxes .....	815
State franchise and sales tax .....	120
	<b>5,545</b>

**NET INCOME BEFORE FEDERAL INCOME TAX .....** **\$ 7,036**

**FEDERAL INCOME TAX .....** **1,548**

**NET INCOME FOR THE YEAR .....** **\$ 5,488**

**RETAINED EARNINGS:**

At beginning of the year ..... 1,744

**AT END OF THE YEAR .....** **\$ 7,232**



## Technical Exhibits

TECHNICAL EXHIBITS will be housed in the Hotel Biltmore's Rex Room, located directly below the Biltmore Bowl and reached by escalator. Here the many exhibitors will present their products and services for members of the Association.

All exhibits and all products exhibited have been screened by a committee as a means of eliminating those which do not meet high standards. The exhibitors agree to this procedure and agree that by this means each will be in good company.

Here in one area will be found the latest developments in

drugs, equipment and services to aid the physician in his professional activities. All physicians are urged to visit the exhibits; meetings have been planned to allow ample time for this important activity. Your visit will not only help bring your own knowledge up to date; it will demonstrate to our exhibitors, who contribute so much to the success of the meeting, that we recognize and appreciate their fine cooperation.

Exhibits are open from 9 a.m. to 5 p.m. each day, Sunday through Tuesday, with an early closing on Wednesday.

### ABBOTT LABORATORIES North Chicago, Illinois

Booth 66

ABBOTT LABORATORIES invites you to visit our exhibit. Our representatives will be happy to answer any questions you may have concerning our leading products and new developments.

### ALTA-DENA DAIRY City of Industry

Booth 35

CERTIFIED MILK, will be served, taste the difference. Produced clean, disease free, antibiotic free, and guaranteed safe through daily laboratory tests conducted under supervision of Los Angeles County Medical Association Milk Commission for over 56 years.

KEFIR: Medical reports indicate good results in normalizing intestinal function following antibiotic therapy. This cultured milk is seeded with *L. Acidophilus* and other friendly lactobacters.

Medical Milk Commission Laboratory reports are made available at each convention for your inspection—your questions will be answered by representatives.

### AMERICANA CORPORATION Beverly Hills

Booth 44

See the newly revised 1965 AMERICANA ENCYCLOPEDIA and MIN/MAX TEACHING MACHINE.

### AQUA TEC CORPORATION Denver, Colorado

Booth 4

AQUA TEC CORPORATION will have personnel on hand to demonstrate WATER PIK, Personal Oral Hygiene Appliance.

### ARNAR-STONE LABORATORIES, INC. Mount Prospect, Illinois

Booth 50

AMERICAINE TOPICAL ANESTHETIC—20 per cent dissolved benzocaine in a water-soluble base—ointment, liquid, suppositories and aerosol forms. Aerosol operates rightside up or upside down for contortion free application. HAZEL-BALM—cooling, soothing witch hazel and emollient lanolin in aerosol form—provides a comforting "cushion of foam." Wide range of usefulness in office and hospital practice.

TETRASULE—prolonged protection against attacks of angina pectoris—b.i.d. dosage of PETN with or without sedation.

### ASTRA PHARMACEUTICAL PRODUCTS, INC. Worcester, Massachusetts

Booth 27

Information and descriptive literature pertaining to XYLOCAINE® (lidocaine) and CITANEST® (propitocaine) local and topical anesthetics, and iron preparations ASTRAFER® (dextriferron) for intravenous use and JEC-TOFER® (iron sorbitex) for intramuscular administration will be available at the ASTRA booth presided over by our representative, Mr. Eric V. Ericson.

### AUDIO-DIGEST FOUNDATION Pacific Medical Equipment Co. North Hollywood

Booth 89

AUDIO-DIGEST FOUNDATION (a non-profit subsidiary of the California Medical Association) gives the busy physician a time-saving tour through the best of some 600 current medical journals, plus the highlights of scores of national meetings. Time-proven, but still unique—these medical tape-recorded services are now offered in seven series—*General Practice, Surgery, Internal Medicine, Obstetrics & Gynecology, Anesthesiology and Ophthalmology*.

Digest subscribers listen in their car, home or office. Carefully selected tape equipment for playing the Digests is offered at the convention by Pacific Medical Equipment Co.

### AYERST LABORATORIES Los Angeles

Booths 64 & 73

We invite all physicians to visit each of the AYERST Exhibits at the annual California Medical Meeting. One exhibit will feature PENBRITIN, the new broad spectrum penicillin effective against both gram negative and gram positive bacteria, the other exhibit featuring PREMARIN and the new concept, as well as other AYERST specialties.

### BARNES-HIND LABORATORIES Sunnyvale

Booth 46

BARNES-HIND LABORATORIES will exhibit their complete line of HEB-CORT creams and lotions, brand of hydrocortisone creams and lotions, and TRANQUINAL (acetyl-carbromal 0.13 gm, bromisovalum 0.25 gm, scopolamine hydrobromide 0.10 mg) the ideal daytime sedative. Complete information and product literature may be obtained at Booth No. 46.

### DON BAXTER, INC. Glendale

Booth 74

DON BAXTER will exhibit the first complete "System" for use in urological irrigating procedures.

Several new products for I.V. Therapy will also be featured.

### BERKELEY MEDICAL INSTRUMENTS Berkeley

Booth 75

A new and simplified method for accurate hemoglobin, glucose, uric acid, cholesterol and B.U.N. determinations in the doctor's office or in the laboratory. Highly reliable results available in minutes. Simplified procedures. Very inexpensive operations.

The instrument is compact, rugged and completely transistorized. These units are in regular use in doctors' offices, laboratories, medical schools, and hospitals.

**BREON LABORATORIES INC.**  
New York, New York

Booth 29

BREON LABORATORIES INC. presents a full line of products for the care of patients with chronic obstructive pulmonary diseases.

Included are BRONKOMETER, BRONKOSPRAY, BRONKOTABS, BRONKOTAB ELIXIR and BRONKEPHRINE. Supplying a variety of formulas, dosage forms and actions; these products offer both prophylaxis and therapy, in chronic or acute conditions, to all ages. BREON personnel will gladly discuss specific products and therapies with you.

**BRISTOL LABORATORIES**  
Syracuse, New York

Booth 16

BRISTOL LABORATORIES' exhibit features TEGOPEN (sodium cloxacillin monohydrate). Unlike penicillin V or G, TEGOPEN eradicates streptococci, pneumococci, staphylococci, and resistant staphylococci; and is priced comparable to quality brands of penicillin V and G. TEGOPEN is available in three dosage forms: 250 mg capsules, oral solution, and 125 mg pediatric capsules.

**THE BROWN PHARMACEUTICAL COMPANY** Booth 31  
Los Angeles

The products the BROWN PHARMACEUTICAL COMPANY will exhibit are: ANDROID, ANDROID H.P., ANDROID X, ANDROID PLUS.

Double blind studies on the use of ANDROID in the treatment of impotence will be available. Also, double blind studies on the use of CEREBRO-NICIN, a cerebro stimulant and vasodilator will be available. Other products will be: GLUKOR, LIPO-NICIN, GERAMINE.

Samples will be given to interested physicians or sent to their home.

**BURROUGHS WELLCOME & CO. (U.S.A.) INC.** Booth 67  
Tuckahoe, New York

You are cordially invited to visit us for information on our products and the newest developments from the research facilities of BURROUGHS WELLCOME & CO.

**BURTON, PARSONS & COMPANY, INC.** Booth 92  
Washington, D.C.

You are cordially invited to stop at the BURTON, PARSONS & COMPANY exhibit where our representative will be showing KONSYL, L. A. FORMULA, NEUTRAcarb and EKG SOL. Samples, descriptive literature, and information will be available on all these products. KONSYL and L. A. FORMULA are the original refined psyllium bulk laxatives. NEUTRAcarb, the antacid available in five delightful flavors, cherry, lemon, lime, peppermint, raspberry. EKG SOL is the original electrode cream for electrocardiography and electroencephalography.

**CARNATION COMPANY** Booth 90  
Los Angeles

The product to be featured will be the new INSTANT BREAKFAST.

**CASS & JOHANSING** Booth 100  
Los Angeles

Representatives will be present to discuss approved County Medical Association Insurance Programs—Professional Liability, Group Disability, Non-Cancellable Disability, Life and Accidental Death & Dismemberment.

In addition, assistance in complete insurance programming will be available.

**CIBA PHARMACEUTICAL COMPANY** Booths 18 & 19  
Summit, New Jersey

The exhibit will highlight the Professional Information Services available from CIBA to the medical profession. These services include Physical Diagnosis Films, Scientific Films, Projection Slides of Medical Illustrations, Clinical Symposia, The CIBA Collection of Medical Illustrations (by Frank H. Netter, M.D.).

**THE COCA-COLA COMPANY** Booth 81  
Atlanta, Georgia

"Ice-cold COCA-COLA served through the courtesy and cooperation of THE COCA-COLA BOTTLING COMPANY of Los Angeles, and THE COCA-COLA COMPANY."

**COLE PHARMACAL COMPANY, INC.** Booth C  
St. Louis, Missouri

COLE PHARMACAL COMPANY will feature IODO-NIACIN and its role in arteriosclerotic, bronchial and sinusitis therapy. See new anatomical art. Helpful information on AS-MINYL, PYRA-GESIC and BANALG and other select COLE products will be available.

**CORECO RESEARCH CORPORATION** Booth 43  
New York, New York

The CORET CAMERA embodies the principle of electronic flash and constant automatic control of such factors as distance, aperture, field, and exposure. Now, for the first time, CORECO offers a completely automatic professional clinical camera purposely designed to achieve the ultimate in surface, intra-oral, and intra-tubular photography. Because of the simplicity of operation, even an inexperienced doctor or nurse can achieve consistently perfect color transparencies.

**CUTTER LABORATORIES** Booth 41  
Berkeley

The CUTTER LABORATORIES booth will feature tangible evidence of the laboratories' leadership in human blood fractions, research and manufacturing. This evidence includes HYPER-TET™ (Tetanus Immune Globulin-Human), HYPERTUSSIS® (Pertussis Immune Globulin-Human), HYPAROTIN® (Mumps Immune Globulin-Human), and GAMASTAN® (Immune Serum Globulin-Human). BREND (noscipine) a new chewable cough suppressant and other prescription specialty products will also be presented.

**DAIRY COUNCIL OF CALIFORNIA** Booth 63  
Sacramento

"AGE MAKES A DIFFERENCE IN CALORIE NEEDS"—A presentation of changing calorie needs throughout life with relation to activity and age. Four food groups emphasize that whatever the age and calorie needs, selective food choices are important.

Nutrition education materials will be displayed that are available, without charge, for helping to reinforce diet instructions to patients.

**DAYLIN MEDICAL & SURGICAL SUPPLY, INC.** Booth 48  
Huntington Park — San Francisco

One source for all your needs—The DAYLIN line of fine pharmaceuticals:

EQUIPMENT — INSTRUMENTS — SUPPLIES

Franchised distributor for the best in the health industry.



DIAPULSE CORPORATION OF AMERICA  
New York, New York

Booth 49

DIAPULSE therapy provides safe, effective treatment through stimulation of normal body defenses. DIAPULSE is of particular value in increasing peripheral blood flow and accelerating wound healing.

DOME LABORATORIES  
New York, New York

Booth 53

DOME LABORATORIES, Division of MILES LABORATORIES INC., world leader in dermatologicals will feature dermatological specialties that are of interest to the members of the California Medical Association. Topical steroid products as CORT-DOME®, NEO-CORT-DOME®, DOMEFORM-HC®, LIDA-MANTLE-HC and COR-TAR-QUIN™ will be presented. We will feature DOME's new antidandruff scalp lotion SCANDAN™. SCANDAN is a clear, nonstaining, non-greasy and nonsticky liquid, for the scalp between shampoos.

We will also feature at this meeting, ALLPYRAL®, DOME's exclusive line of alum precipitated pyridine extracts.

D. M. DOYLE PHARMACEUTICAL COMPANY Booth 30  
A Division of The Dietene Company  
Minneapolis, Minnesota

Have you tasted MERITENE? MERITENE is the good-tasting protein-vitamin-mineral food supplement prescribed to provide concentrated nutrition for patients with poor appetite or tolerance for ordinary food. Visit our booth and let us serve you a cool, refreshing MERITENE Nourishment.

While there, review also our DIETENE Reducing Plan, designed to get better cooperation from over-weight patients. The DIETENE Plan provides optimum nutrition and maximum satiety without the use of drugs.

MERITENE and DIETENE are advertised only to the medical profession.

ENCYCLOPAEDIA BRITANNICA  
Chicago, Illinois

Booth 96

ENCYCLOPAEDIA BRITANNICA welcomes delegates to the California Medical Association meeting and invites them to examine the great new edition of BRITANNICA.

Official delegates may now purchase this magnificent set at an offer only available at our convention exhibits. Visit BRITANNICA's Booth No. 96.

ENDO LABORATORIES INC.  
Garden City, New York

Booth 91

ENDO LABORATORIES will present the latest clinical information relating to our products, PERCODAN®, PERCOGESIC-C®, PERCODAN®-DEMI, COUMADIN® (warfarin sodium), NUMORPHAN® (oxymorphone) HCL, HYCOMINE®, HYCOMINE®-COMPOUND, HYCODAN®, VALPIN® (anisotropine methylbromide), VALPIN®-PB (anisotropine methylbromide with phenobarbital).

FELLOWS-TESTAGAR  
Detroit, Michigan

Booth 45

FELLOWS-TESTAGAR features: AMODEX TIMED CAPSULES (anorexigenic); PENTRYATE TIMED CAPSULES (vasodilator) and FEMOGEN Tablets (conjugated estrogens). Of special interest will be our new sampling technique—the Rx AMPLE PROGRAM—the modern and convenient physician starter sample method.

Stop by for an official copy of the HR-2 Drug Abuse Law.

FELLOWS-TESTAGAR also celebrates their Centennial Year. Fellows Medical Mfg. Co., Inc., has been in continual operation since 1866.

CHARLES O. FINLEY & COMPANY, INC.  
Los Angeles

Booth 3

CALIFORNIA MEDICAL ASSOCIATION DISABILITY INSURANCE PROGRAM—Protect your most valuable asset, "Your Earning Power." New rates for the younger doctor. Applicants to California Medical Association are now eligible to apply. Private flying now covered.

FLINT LABORATORIES  
Morton Grove, Illinois

Booth 28

Featured products are SYNTHROID® and HU-TET™. . . SYNTHROID (sodium levothyroxine) tablets and injection, the active principle of the thyroid gland, prepared synthetically in pure crystalline form for predictable and stable therapeutic results.

HU-TET (Tetanus Immune Globulin-Human), tetanus antitoxin of human origin for virtual freedom from sensitivity reactions. Now available from FLINT LABORATORIES in 250 unit vials for economical and long-lasting protection.

FULLER PHARMACEUTICAL COMPANY  
Minneapolis, Minnesota

Booth 62

GEIGY PHARMACEUTICALS  
Yonkers, New York

Booth 14

GEIGY PHARMACEUTICALS cordially invites members and guests of the Association to visit its exhibit. The exhibit features important new therapeutic developments in the management of cardiovascular disease as well as current concepts in the control of inflammation; hypertension and edema; depression; obesity, and other disorders, which may be discussed with representatives in attendance.

GERBER BABY FOODS  
Fremont, Michigan

Booth 37

You are cordially invited to visit our exhibit. You will be briefly but reliably informed of recent developments in the only complete line of infant foods. New editions of "Nutritive Values" and "Ingredients" of GERBER baby foods are among a number of specialized services available for your office. Attractive packets of individualized food lists for your food-sensitive babies are just off the press and ready for your order. Please stop by.

GREAT BOOKS with The SYNTOPICON  
Chicago, Illinois

Booth 34

THE GROlier SOCIETY, INC.  
Los Angeles

Booth 32

Brand-new edition of the world-famous BOOK OF KNOWLEDGE, available at a special exhibit offer for members only.

GUARDIAN CHEMICAL CORPORATION  
Long Island City, New York

Booth 2

The company will exhibit the following pharmaceutical specialties:

RENACIDIN—for irrigating indwelling urethral catheters and the urinary bladder to prevent or remove encrustations due to calcification.

PHOS-PHaid—for urinary acidification in order to in-

crease calcium solubility and assist in preventing formation of calcifications in the urinary tract.

**LUBRASEPTIC JELLY**—the anesthetic, antibacterial, water-soluble lubricant.

**CLORPACTIN WCS-90** (sodium oxychlorosene) for use in the prevention of postoperative infections and in the treatment of infections which are antibiotic resistant.

**CLORPACTIN XCB** (oxychlorosene)—for use in destroying viable tumor cells during cancer surgery for the purpose of minimizing local recurrences.

**J. H. HEDRICK & CO.**  
San Gabriel

Booth 26

Designers and builders of medical-dental buildings as well as other office buildings, motels, and apartments. Home office in San Gabriel, California. Branch offices in South San Francisco, Santa Barbara, Ventura, and San Diego, California.

**JACUZZI RESEARCH INC.**  
Berkeley

Booth 42

Demonstration of portable JACUZZI WHIRLPOOL BATH for use in hydrotherapy treatments in hospitals, nursing homes and clinics. The JACUZZI WHIRLPOOL BATH will be shown in use in a plastic pool. Exhibit also includes technical photos and literature depicting the uses and benefits of JACUZZI WHIRLPOOL BATH.

**THE JOBST INSTITUTE, INC.**  
Toledo, Ohio

Booth 8

JOBST custom-made Venous Pressure Gradient Supports prescribed by leading vascular specialists for the treatment and control of vascular disorders such as varicose veins, the post-phlebitis syndrome, chronic venous insufficiency and lymphedema of the extremities. The JOBST Intermittent Compression Units are used in the treatment of massive and obstinate lymphedema of the extremities such as postmastectomy lymphedema and lymphedema due to node dissection. Intermittent Compression Units and Pneumatic Appliances are available on rental for home use.

**KENWOOD LABORATORIES, INC.**  
New Rochelle, New York

Booth 61

Featured in our display is PAPAVALTRAL, a vasodilator, pentaerythritol tetranitrate and smooth muscle relaxant, ethylpapaverine HCL (ethaverine hydrochloride) for the aid in the treatment of Angina Pectoris and Peripheral vascular diseases. PAPAVALTRAL is supplied both in tablets 10 mg and 20 mg. Also long-acting capsules.

**KEY PHARMACEUTICALS, INC.**  
Miami, Florida

Booth D

NITROGLYN - PROPERNOL - HYASORB - SEDUTIN - THEONAR - CARBAMINE - NITROGLYN-SUBLINGUAL.

**LEDERLE LABORATORIES**  
Pearl River, New York

Booth 6

LEDERLE LABORATORIES, one of the leaders in medical research and development, is proud to support the 1966 Annual Session of the California Medical Association. Our sales representatives in Booth No. 6 are qualified to discuss products such as DECILOMYCIN®, ACHROMYCIN®V, ARISTOCORT®, AMICAR®, as well as our many services to physicians. We hope to be of service to your practice.

**ELI LILLY AND COMPANY**  
Indianapolis, Indiana

Booth 33

You are cordially invited to visit the LILLY exhibit. Our sales representatives in attendance welcome your questions about LILLY products. You may be particularly interested in discussing KEFLIN® cephalothin, or C-QUENS™ Sequential folder containing fifteen 80-mcg tablets of mestranol plus five tablets each combining 80 mcg mestranol and 2 mg chlormadinone acetate.

**LOMA LINDA FOODS**  
Riverside

Booth 72

LOMA LINDA FOODS, manufacturers of the tasty hypoallergenic infant soy milk, SOYALAC, will be pleased to show evidence of the nutritional adequacy of their product. The company is America's exclusive manufacturer of fiber-free soy milk. Qualified attendants will be pleased to explain why this milk is unusual in that it does not tend to raise infants' serum cholesterol. Uses of this milk for adult ulcer patients and in cholesterol-lowering diets will be discussed. Samples of this flavorful product will be served.

**McNEIL LABORATORIES, INCORPORATED**  
Fort Washington, Pennsylvania

Booth 84

Members of the California Medical Association are cordially invited to visit our Booth No. 84. Products to be featured are: BUTISOL SODIUM® (sodium butabarbital), PARAFON FORTE® and TYLENOL® (acetaminophen).

**MEAD JOHNSON LABORATORIES**  
Evansville, Indiana

Booth 83

The MEAD JOHNSON LABORATORIES' exhibit has been arranged to give you the optimum in quick service and product information. To make your visit productive, specially trained representatives will be on duty to tell you about their products.

**MEDCO PRODUCTS CO.**  
Tulsa, Oklahoma

Booth 25

MEDCO's direct reading instant thyroid test.

The MEDCO ACHILLEOMETER is a solid state (transistorized) Achilles Reflex Test (A.R.T.) Computer. Permits immediate and accurate diagnosis—answers the problem of the borderline Hypo-Thyroid and response to therapy.

As no electrocardiograph is necessary, the ACHILLEOMETER offers the Achilles Reflex Test (A.R.T.) method of testing thyroid function to many additional physicians. Compact, (5½ lbs.), no warm-up period, desk-top convenience.

**MEDICAL MANAGEMENT CONTROL**  
San Francisco

Booth 93

Member: Society of Professional Business Consultants.

Material and information on the four major areas of service to which MEDICAL MANAGEMENT CONTROL devotes itself exclusively in serving the physicians' needs in the management of solo, partnership, group or association practice. These areas include:

1. Practice management consultation—Including book-keeping services, tax and financial planning and control.

2. Facilities management—Including feasibility studies, planning construction, creating, supervising, and reorganization of medical arts centers.

3. General and special surveys of solo, partnerships, groups and associations.

4. Partnership, group and association management—



Including business advice on formation of such groups and follow-through procedures to insure successful operation.

**THE MEDICAL PROTECTIVE COMPANY**                      **Booth 36**  
Fart Wayne, Indiana

**MERCK SHARP & DOHME**                                      **Booth 82**  
West Point, Pennsylvania

The MERCK SHARP & DOHME exhibit has been designed to supplement the physicians therapeutic armamentarium. Technically trained personnel are present to discuss the scope and variety of services offered.

**MILEX-FERTILEX CO.**    **Booth 99**  
Las Angeles

Ask for your sample copy "*Personal Understanding of Marriage*," by Dr. Robert Rutherford and Jean Rutherford. A total of seven Doctor-to-Patient titles now available.

**MISSION PHARMACAL COMPANY**                              **Booth 103**  
San Antonio, Texas

MISSION PHARMACAL COMPANY will be displaying new HOMAPIN® LIQUITAB™ (homotropine methylbromide), the first chewable, flavored antispasmodic to be marketed in the United States. Also featured will be PRULET® LIQUITAB™, a flavored, chewable form of Mission's very popular PRULET laxative tablets.

Other well known products of MISSION manufacture are EQUILET® antacid tablets; FOSFREE® for nocturnal leg cramping; SUPAC®, a non-narcotic analgesic compound; FETAMIN® (methamphetamine and phenobarbital with vitamins) for sensible weight control; and IROMIN-G®, a hematonic supplement.

**THE NATIONAL DRUG COMPANY**                              **Booth 60**  
Division of Richardsan-Merrell Inc.  
Philadelphia, Pennsylvania

THE NATIONAL DRUG COMPANY will exhibit new AVC DIENESTROL for atrophic vaginitis complicated by infection; TEPANIL TEN-TAB (diethylpropion hydrochloride continuous release form) indicated for day-long reduction of appetite as an aid in any weight-reduction program, even for diabetics, hypertensives and cardiacs; ORENZYME, the original oral proteolytic enzyme for reduction of inflammation and edema; and AVC IMPROVED for comprehensive vaginal anti-infective therapy.

**NEELY SALES DIVISION**    **Booth 69**  
Hewlett-Packard  
North Hollywood, California

SANBORN DIVISION, HEWLETT-PACKARD—Model 500 Electrocardiograph with matching mobile cart and 1506A Heart Sound Amplifier. Model 75 Blood Cell Counter and new Model 74 Auto-diluter. Model S1000 Blood Analyzer for cholesterol, hemoglobin, glucose and uric acid determinations. Also, SANBORN's complete new line of Model 780 patient monitoring and resuscitation equipment for intensive care, recovery and emergency rooms. The Model 780 units are of modular construction and are complete with carts, transducers, brackets and cabling for a complete, integrated system.

**THE NETTLESHIP COMPANY OF LOS ANGELES**              **Booth A**  
Las Angeles

Administrators of Professional Liability, Group Accident and Sickness, and Life Insurance Programs for County Medical Associations and Trusts in California.

Qualified representatives available to discuss problems pertaining to hospital or individual professional liability coverage, accident and sickness, life, or other types of insurance.

Literature, which will assist in the prevention of claims and various forms to be used to protect, as far as possible, against malpractice claims.

**NEUTROGENA CORP.**    **Booth 95**  
Santa Monica

NEUTROGENA SOAP is a mild, transparent, ethanalamine-base soap and contains no free alkali. It is not a detergent nor is it medicated; yet so different it was granted a U.S. patent (No. 2,820,768). NEUTROGENA is mild, non-drying, and non-irritating. It is well-tolerated in cases of common dermatitis, eczema, acne and other skin problems . . . especially where washing with soap is contra-indicated.

**NIAGARA THERAPY MANUFACTURING CORPORATION**    **Booths 76 & 77**  
Las Angeles  
CYCLO-MASSAGE products.

**ORGANON INC.**    **Booth 88**  
West Orange, New Jersey

ORGANON INC. invites you to Booth No. 88 where skilled representatives will demonstrate the newest developments in endocrinology. Your questions and comments are invited.

**ORTHO PHARMACEUTICAL CORPORATION**                      **Booths 1 & 97**  
Raritan, New Jersey

Welcome to Booth No. 1 where ORTHO® is proud to present the most complete line of medically accepted products for the control of conception. Of special note are the two latest products of the ORTHO Research Foundation, ORTHO-NOVUM® tablets and DELFEN® Vaginal Foam.

Also on display in Booth No. 97 will be our well-known products for treatment of various forms of vaginitis.

Your questions will be welcomed by representatives in attendance.

**OXFORD FURNITURE DISTRIBUTING CO.**    **Booths 101 & 102**  
Las Angeles

The OXFORD THERMASSAGE CHAIR—A tilt-back, oscillating, massage chair with soothing heat and roller-massager back.

**PARKE, DAVIS & COMPANY**    **Booth 94**  
Detroit, Michigan

Medical service members of our staff will be in attendance at our booth to discuss important PARKE-DAVIS specialties which will be on display.

**PASADENA RESEARCH LABORATORIES, INC.**                      **Booth 59**  
Pasadena

Representatives from several areas of the State of California will be in attendance at our booth to greet the members of the California Medical Association and to discuss the merits of some of our fine products with them.

**PFIZER LABORATORIES**    **Booth 12**  
New York, New York

**PITCHER ELECTRONICS, INC.**  
Brea

Booth 57

Portable X-Ray and Physical Medicine equipment by SIEMENS, builders of the world's finest medical equipment. Factory personnel in attendance at the booth.

**PLEASURE TOY HOUSE**  
Fontono

Booth 40

BEHAVIOR INCENTIVES—For the professions only. Selected and individually packaged toy guaranteed to please your "little patients."

Princess Ann American-made rings, as pretty as mom's; Spinner, twistee, imprint balloons; Itty Bitty's and many, many more high-quality, low-cost toys for girls and boys.

**PROCTER & GAMBLE COMPANY**  
Cincinnati, Ohio

Booths 85 & 86

Booth will feature SAFEGUARD—PROCTER & GAMBLE's new anti-bacterial bar soap that can be of significant value wherever suppression of bacterial skin flora is indicated.

**RIKER LABORATORIES**  
Northridge

Booth 9

Representatives of RIKER LABORATORIES will be glad to supply you with complete information concerning our products which are available to the medical profession. Please feel free to request answers to any questions you may have. We will be looking forward to your visiting our booth.

**RITTER EQUIPMENT COMPANY**  
Rochester, New York

Booth 51

Let Pat Kelly or Lew Cook demonstrate the new LIEBEL-FLARSHEIM manufactured Uniflex Diathermy to you. The unique Applicator is ideal for either local or long-path treatment—no more changing applicators.

Also on display will be the RITTER 75 and 45 Power Tables—one is right for your practice.

See also the colorful Model 7 SPEEDCLAVE, the BANTAM BOVIE, and the No. 8 Lamp.

**A. H. ROBINS COMPANY, INC.**  
Richmond, Virginia

Booth 13

You are cordially invited to visit the ROBINS display and meet our representatives who will be happy for the opportunity to discuss products of interest to you.

**ROCHE LABORATORIES**  
Nutley, New Jersey

Booth 24

Continuing ROCHE research has produced outstanding contributions to medicine since 1909. The personnel at the exhibit welcome your comments, questions or suggestions about our products and services.

**J. B. ROERIG & COMPANY**  
New York, New York

Booth 11

Representatives of J. B. ROERIG & COMPANY will be glad to supply you with complete information concerning our products which are available to the medical profession. Please feel free to request answers to any questions you may have. We will be looking forward to your visiting our booth.

**SANDOZ PHARMACEUTICALS**  
Honover, New Jersey

Booth 54

SANDOZ PHARMACEUTICALS cordially invites you to visit our display at Booth No. 54, where we are featuring

MELLARIL, SANSERT, CAFERGOT P-b, FIORINAL and FIORINAL with codeine.

Any of our representatives in attendance will gladly answer questions about these and other SANDOZ products.

**W. B. SAUNDERS COMPANY**  
Philadelphio, Pennsylvania

Booth 79

New SAUNDERS books since last year's meeting include: Bockus: *Gastroenterology*, 2nd ed., Vol. III; Gellis and Kagan: *Pediatric Therapy*; Ingelfinger et al.: *Controversy in Internal Medicine*; Conn, Clohecy and Conn: *Current Diagnosis*; Friedberg: *Diseases of the Heart*; and Conn: *1966 Current Therapy*.

**SCHERING CORPORATION**  
Bloomfield, New Jersey

Booths 70 & 71

SCHERING CORPORATION invites you to visit their Doctor-to-Doctor Convention Center. At this Center, physicians representing SCHERING CORPORATION will be available to discuss the company's latest medical services including teaching aids (slides, films and literature) and to answer questions concerning drug therapy with practitioners and those engaged in research. In the adjacent booth, No. 70, our SCHERING representatives will be available to discuss with you any questions you may have on AFRIN®, TIN-ACTIN®, CELESTONE®, SOLUSPAN™ or any other SCHERING product.

**G. D. SEARLE & CO.**  
Chicago, Illinois

Booth 23

You are cordially invited to visit the SEARLE booth where our representatives will be happy to answer any questions regarding SEARLE Products of Research.

Featured will be ENOVID for ovulation control and pregnancy and menstrual disturbances; and FLAGYL, a potent, new trichomonacidal agent for trichomonal vaginitis, cervicitis, urethritis and prostatitis.

**SEVEN-UP BOTTLING COMPANY OF  
LOS ANGELES, INC.**  
Los Angeles

Booth 47

**SHELLEY PROFESSIONAL PRODUCTS, INC.**  
Los Angeles

Booth 98

A suite of SHELLEY "Futura" Examining Room Equipment and Modular cabinetry will be displayed in beautiful royal walnut with contrasting upholstery. Every piece of the examining room set is brilliantly styled and completely laminated with LIFETIME FORMICA—marproof—stainproof—will look New for years to come. Examining tables — cabinets — waste receptacles — operator's stools. See them on display at our booth. It's A MUST!

**SIEMENS MEDICAL OF AMERICA INC.**  
Burlingome

Booth 58

SIEMENS MEDICAL will display the complete SIEMENS line. Different new developments for therapy and diagnosis will be shown and our representatives will be on hand to answer any questions you may have.

Few minutes at our booth may prove to be of great value to you.

**SMITH KLINE & FRENCH LABORATORIES**  
Philadelphio, Pennsylvania

Booth 52

Representatives will be on hand to answer your specific questions, and provide information on their products and services.



**SMITH, MILLER & PATCH, INC.**  
New York, New York

Booth 78

SMITH, MILLER & PATCH, INC. cordially invites you to visit their exhibit. Our representatives will be pleased to discuss the latest advances in therapy. Featured at our exhibit will be: CEPHALGESIC, a new product for the treatment of headache; LIPOFLAVONOID, LIPOTRIAD, VITRON-C and KONDREMUL. Also featured will be a range of topical ophthalmic preparations including VASCON-A, an antihistamine/decongestant.

**SOCIETY OF MEDICAL FRIENDS OF WINE**  
San Francisco

Booth E

The SOCIETY OF MEDICAL FRIENDS OF WINE will sponsor an exhibit of the dietary and therapeutic values of wine, at which there will be available copies of the *Uses Of Wine In Medical Practice*, a summary of the results of 25 years of research on the chemical constituents, physiological effects and health values of wine.

**SOLANO LABORATORIES**  
Berkeley

Booth B

Laboratory services offered to the medical profession—automated and referral tests. A complimentary “annual survey”—health evaluation via laboratory analysis—will be offered to the physician.

**E. R. SQUIBB & SONS**  
New York, New York

Booth 5

E. R. SQUIBB & SONS has long been a leader in development of new therapeutic agents for prevention and treatment of disease. The results of our diligent research are available to the Medical Profession in new products or improvements in products already marketed.

At Booth 5, we will be pleased to present up-to-date information on these advances for your consideration.

**STACEY'S**  
Palo Alto, San Francisco, Denver

Booth 15

STACEY'S, the largest distributor of medical books in America, will be in attendance with a large display featuring the latest important books from all medical publishers, plus up-to-the-minute information about forthcoming books in each specialty. If you have not received your free copy of *Medical Books in Print*, be sure to stop by STACEY'S booth and pick one up.

**THE STUART COMPANY**  
Pasadena

Booths 21 & 22

A cordial invitation is extended to all members and guests attending this meeting to visit the STUART COMPANY booth. Specially trained representatives will be in attendance to answer your questions on new products, developed in our modern laboratories, which have particular interest for the medical profession. Products featured are DIALOSE, DIALOSE PLUS, MYLICON, MYLANTA, STUART PRENATAL, STUART PRENATAL-F, MULVIDREN-F and MULVIDREN JUNIOR.

**SWIFT & COMPANY**  
Chicago, Illinois

Booth 65

SWIFT'S Baby Foods—100 per cent meats, high meat dinners and egg yolks are featured at the SWIFT exhibit. Also on display are Jr. franks and chicken sticks specially prepared for toddlers. Attractive *Mother Booklets* are available on request as well as literature evaluating meat in the infant diet and other nutritional information on SWIFT'S Baby Foods.

**SYNTEX LABORATORIES, INC.**  
Palo Alto

Booths 10 & 68

SYNALAR® (fluocinolone acetonide), the topical corticosteroid designed to meet specific dermatologic needs, will be featured at Booth No. 10. SYNALAR has set a new standard of success in the treatment of a wide range of inflammatory dermatoses.

A warm invitation is extended to all physicians attending this meeting to visit our booth and discuss the latest developments from SYNTEX research.

NORINYL® (norethindrone 2.0 mg with mestranol 0.1 mg) tablets, an original steroid from SYNTEX LABORATORIES, will be featured at Booth No. 68. NORINYL 2 mg super-sedes barrier methods of contraception.

Physicians are invited to register at the SYNTEX exhibit for complete information on this outstanding new product.

**3M BUSINESS PRODUCTS SALES INC.**  
Los Angeles

Booth F

3M Company's newest Bookkeeping and Billing System.

**TRU-EZE MANUFACTURING CO., INC.**  
Burbank

Booth 87

TRU-EZE will be exhibiting the newest TRU-TRAC electrically controlled portable intermittent traction machine and the “all new” redesigned TRACTOMATIC II.

Also demonstrated will be the RT-99 Friction-Free traction and therapy table FTC-20 Multi-Angle flexion chair, and the versatile TS-93 traction stand. Ultimate convenience is afforded by the LIQUI-TRAC traction weight bag on display and now available from TRU-EZE in 10 and 20 pound capacity as well as a diversified assortment of home traction & therapy devices.

**THE UPJOHN COMPANY**  
Kalamazoo, Michigan

Booths 55 & 56

Professional representatives of THE UPJOHN COMPANY are eager to contribute to the success of your meeting. We are here to discuss with you products of UPJOHN research that are designed to assist you in the practice of your profession. We solicit your inquiries and comments.

**U.S. VITAMIN & PHARMACEUTICAL CORP.**  
New York, New York

Booth 20

The U.S. VITAMIN & PHARMACEUTICAL CORPORATION cordially invites you to visit their exhibit where ARLIDIN will be on display, as well as other leading pharmaceutical specialties and nutritional products.

Professional service representatives will be in attendance to welcome you and to be of help in answering any inquiries pertaining to the products on display, as well as any of their other products.

**WALLACE LABORATORIES**  
Cranbury, New Jersey

Booth 17

We invite you to visit our booth where our representatives in attendance will be pleased to furnish information regarding WALLACE products and your related medical questions to assist you in your practice.

**WESTWOOD PHARMACEUTICALS**  
Buffalo, New York

Booth 39

WESTWOOD invites physicians to stop by their booth to discuss their unique dermatological products:

FOSTEX CREAM, PERNOX, SEBULEX, ALPHA-KERI, FOSTEX CAKE, SEBUTONE, FOSTRIL, KERI LOTION.

These products are particularly suitable for personal use by physicians and their families who may be plagued with dandruff, acne, dry and itchy skin, and sensitivities to soap. Register, so that we may send prescription units to your home.

**WHITE LABORATORIES, INC.**  
Kenilworth, New Jersey

Booth 7

WHITE LABORATORIES' exhibit features an important prescription product — DISOPHROL® CHRONOTAB® tablets. Medical Service Representatives will be happy to discuss the many indications and the superior therapeutic effectiveness of this preparation.

**WTS-PHARMACRAFT**  
Rochester, New York

Booth 38

DESENEX: Most widely prescribed fungicide used in the prevention and treatment of athlete's foot and other superficial fungus infections of the skin.

CALDESENE: Provides a lubricating and emollient film which is effective in the prevention or treatment of diaper rash and minor skin irritations.

**WYETH LABORATORIES**  
Philadelphio, Pennsylvonio

Booth 80

WYETH will feature . . .

NEW SERAX® (oxazepam, WYETH) Capsules—Important new specific for anxiety with broad clinical application, SERAX is notable for the wide separation of effective and side effective doses, is indicated in management and control of anxiety, tension, agitation, irritability and related symptoms. SERAX has great specificity and utility in a wide range of patients. It affords prompt response while at the same time allows the patient to function. Suitable for geriatric use too.

Full information is available at Booth No. 80.

WYETH will also feature . . .

UNIPEN® (sodium nafcillin, WYETH) Capsules and Injection—penicillin of choice for initial therapy in severe or potentially severe gram-positive injections. Provides immediate positive antibacterial action against staphylococci (penicillin-resistant and -susceptible), streptococci and pneumococci.

## QUALIFICATIONS/REQUIREMENTS FOR REGISTRATION

(a) All M.D.'s with credentials showing that they hold valid license to practice medicine. (Membership cord in C.M.A.; county medical society/association or A.M.A. membership cord.)

(b) Medical students will be admitted upon presentation of credentials from their medical schools identifying them as medical students. (A membership cord of the Student American Medical Association or letter from their dean's office.)

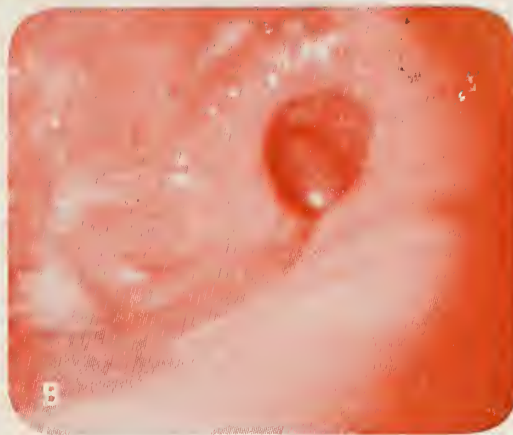
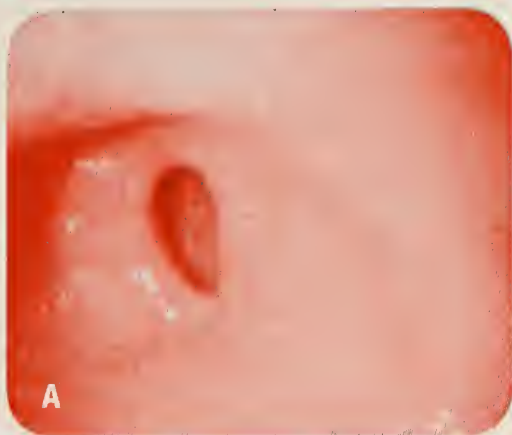
(c) Medical assistants will be admitted upon presentation of a letter from the physician-employer or C.M.A.A. membership cord.

(d) Military paramedical personnel will be admitted upon presentation of a letter requesting their admittance, written by their commanding officer.

(e) Dentists (D.D.S.), doctors of veterinary medicine (D.V.M.), registered nurses (R.N.), student nurses, x-ray technicians, laboratory technicians, allied public health personnel, and others will be admitted provided they have proper identification.

(f) All questions on admission will be passed upon by a member of the Committee on Registration who will be present at the desk.





*Which Is Pyloroplasty with Vagotomy?      Which Is Pro-Banthine?*

## Another example of **Pro-Banthine<sup>®</sup>** (propantheline bromide) a true anticholinergic in action

The true anticholinergic values of Pro-Banthine have never been so graphically realized as they are with the recent development of fibergastroscopy and the intragastric camera.

Pro-Banthine consistently produces complete relaxation and immobility of the stomach with a dose of only 6 to 8 mg. intravenously. This is less than half the usual dose orally.

Atropine, on the other hand, required 0.8 mg. intravenously, or twice the normal dose, to achieve a similar effect. This high dose of atropine resulted in expectedly adverse side effects.

Pro-Banthine, in minimal dosage, produces effects similar to pyloroplasty and vagotomy without the disadvantages of permanent postvagotomy sequelae.

The intra-gastric photograph A above

is of a patient who has had pyloroplasty with vagotomy. Photograph B is of a patient given 6 mg. of Pro-Banthine.

**Indications:** Peptic ulcer, functional hypermotility, irritable colon, pylorospasm and biliary dyskinesia.

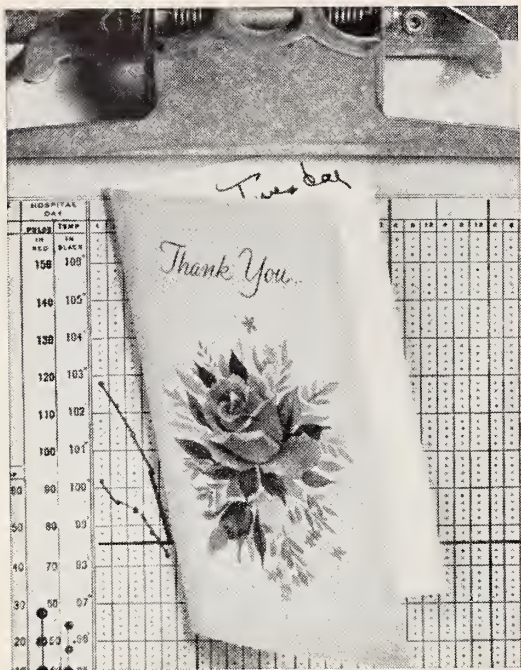
**Oral Dosage:** The maximal tolerated dosage is usually the most effective. For most *adult* patients this will be four to six 15-mg. tablets daily in divided doses. In severe conditions as many as two tablets four to six times daily may be required. Pro-Banthine (brand of propantheline bromide) is supplied as tablets of 15 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type ampuls of 30 mg.

**Side Effects and Contraindications:** Urinary hesitancy, xerostomia, mydriasis and, theoretically, a curare-like action may occur. Pro-Banthine is contraindicated in patients with glaucoma, severe cardiac disease and prostatic hypertrophy.

Photographs—Harry Barowsky, M.D., Lawrence Greene, M.D., and Robert Bennett, M.D., from a Scientific Exhibit presented at the Annual Meeting of the American College of Gastroenterology, Bar Harbour, Florida, Oct. 24-27, 1965.

**SEARLE**

*Research in the Service of Medicine*



## DID YOU EVER GET A "THANK YOU" NOTE FROM A SPECIAL-DIET PATIENT?

It can happen. Get hold of our free booklet and see the remarkable things that can be done with a diet that is built on Cream of RICE.

It's called "How To Make A Special Diet Taste Extra Special!" You'll find delicious recipes for bland, wheat-free, milk-free, egg-free and low-salt diets.

A recent research study compared the breakdown of Cream of RICE with oat, wheat, corn and barley cereals and concluded that Cream of RICE was easiest to digest.

Cream of RICE is fortified with Vitamin B<sub>1</sub>, Riboflavin, Niacin and Iron. And it's low in residue and fat. The patient gets dietary protection, flavor satisfaction and good nutrition. And you may actually get a "Thank you."



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Please send \_\_\_\_\_ (state number desired) free copies of "How To Make A Special Diet Taste Extra Special!" to

Name \_\_\_\_\_

Address \_\_\_\_\_

City \_\_\_\_\_

State \_\_\_\_\_ Zip Code \_\_\_\_\_

## BOOKS RECEIVED

(Continued from Page 32)

by Verne T. Inman, A.B., M.A., Ph.D., M.D. The C. V. Mosby Company, St. Louis, Mo., 1965. 586 pages \$17.50.

**SYMPOSIUM ON CATARACTS**—Transactions of the New Orleans Academy of Ophthalmology—Benjamin F. Boyd M.D.; Leonard Christensen, M.D.; A. Ray Irvine, Jr., M.D.; Murray F. McCaslin, M.D.; P. Robb McDonald, M.D.; John M. McLean, M.D.; and Richard C. Troutman, M.D. The C. V. Mosby Company, St. Louis, 1965. 340 pages, \$19.50.

**THERAPEUTIC RADIOLOGY**—Rationale, technique, results—Second Edition—William T. Moss, M.D., Professor of Radiology, Northwestern University School of Medicine, Department of Radiology, Chicago, Illinois; Director, Department of Therapeutic Radiology, Veterans Administration Research Hospital, Chicago, Illinois. With foreword by Lauren V. Ackerman, M.D. The C. V. Mosby Company, St. Louis, 1965. 514 pages, \$18.75.

**VITREORETINAL PATHOLOGY AND SURGERY IN RETINAL DETACHMENT**—Paul A. Cibis, M.D., Department of Ophthalmology and the Oscar Johnson Institute, Washington University School of Medicine, St. Louis, Missouri. 293 pages, \$20.00.

**YEAR BOOK OF ANESTHESIA (1965-1966 Year Book Series)**—Edited by Stuart C. Cullen, M.D., Professor and Chairman, Department of Anesthesia, University of California Medical Center, San Francisco. Year Book Medical Publishers, Incorporated, 35 East Wacker Drive, Chicago, Ill., 1965. 389 pages, \$8.50.

## Rural Health Conference Scheduled March 18-19

Farm and health leaders will meet March 18-19 at Colorado Springs for the 19th National Conference on Rural Health.

The meeting in the Broadmoor Hotel is sponsored by the American Medical Association's Council on Rural Health together with state medical associations, farm, educational, and allied health organizations.

W. Wyan Washburn, M.D., Chairman of the Council on Rural Health, described the purposes of the Conference as:

- To improve methods of communication in health education for rural people.
- To more fully understand and be able to utilize more efficiently health manpower resources in a community.
- To assess the effect of environmental factors on the health, safety and well-being of people living in rural areas.
- To discover and be able to implement the utilization of community health resources.

Following an address by Governor John A. Love of Colorado, the sessions on the 18th will feature programs to meet health manpower needs, guidelines for better communication, and water pollution control measures in rural areas. The program for the 19th will be highlighted by breakfast discussion groups on a wide range of health subjects, a talk on rural accident prevention, and a review of the work of the National Commission on Community Health Services.

Marion D. Hanks, LL.B., of the Church of Jesus Christ of Latter-day Saints, will speak on the subject "What Rural Youth Needs Today" at the banquet session on Friday evening.



# analysis B

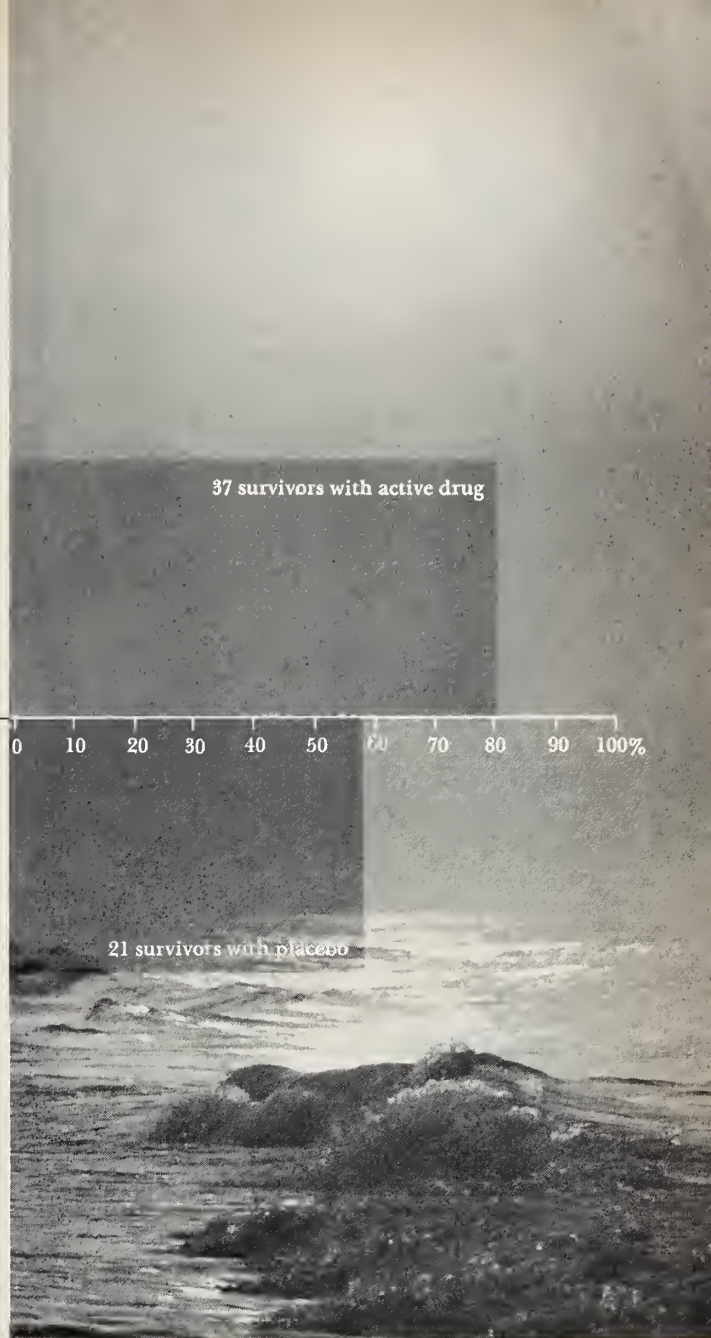
from the original 100 patients  
37<sup>†</sup> survived hospitalization  
of these patients 2 years later<sup>3</sup>...

**80.4%** of 46 patients  
have survived with  
**Peritrate SA**  
(pentaerythritol tetranitrate)  
80 mg. Sustained Action

**58.4%** of 36 patients  
have survived with  
placebo

When mortality data from the 21-day hospitalization period are excluded, the postinfarction survival statistics continue to favor Peritrate (pentaerythritol tetranitrate). In the 2 years following discharge, 9 of the 46 drug-treated patients have died: mortality—19.6%. In the same period, 15 of 36 patients in the placebo group have died: mortality—41.6%.<sup>3</sup>

<sup>†</sup>Of the 87 survivors, 5 were lost to follow-up.



**Peritrate<sup>®</sup> SA**  
(pentaerythritol tetranitrate)  
80 mg. Sustained Action  
...brings more blood and oxygen to the myocardium  
...stimulates development of collateral circulation<sup>4</sup>

Side effects: Negligible but, occasionally, transient headache may occur.

Precautions: Exercise caution in glaucoma and with dosage forms containing phenobarbital, which may be habit forming.

References: 1. Oscharoff, A.: *Angiology* 15:505, 1961. 2. Oscharoff, A.: Paper presented at the Annual Meeting, Michigan Academy of General Practice, Detroit, November 11-12, 1961. 3. Data on file in the Medical Department of Warner-Chilcott Laboratories. 4. Lumb, G. D., and Hardy, L. B.: *Circulation* (Pt. II, Cardiovascular Surgery) 27:717, 1963.



**WARNER-CHILCOTT**

Warner-Chilcott, Morris Plains, N.J.  
Makers of Coly-Mycin Gelusil Mandelamine Proloid Tedral





**Openings in General Medicine  
and Psychiatry  
in State hospitals and  
youth and adult correctional facilities**

Although most vacancies are in the field of psychiatry, there are frequent openings in general medicine in State facilities. These offer opportunity to develop psychiatric skills if interested.

Because of the wide variety in medical and rehabilitation activities in both mental health and correctional institutions, many doctors can broaden their experience in State service, and enter for that reason. Your inquiry is invited.

Write for details to: William F. Webster  
State Personnel Board  
Sacramento, California 95814



## Two Reports On Heart Disease

The relationship of behavior patterns, municipal drinking water and several other factors to heart disease are discussed in two articles in the January 10 *Journal of the American Medical Association*.

One report indicates that the association of softness of municipal water and death rates from hypertensive and arteriosclerotic heart disease, first demonstrated for 1949 to 1951, persisted in 1960. The purer the water in terms of dissolved elements, the higher the death rate from these causes, the report said.

In the second report, a two and a half year follow-up of 3,524 California men aged 39 to 59 indicates there is increased likelihood of coronary heart disease among those who are particularly ambitious, aggressive, competitive, and worry about deadlines in their work.

These active, aggressive men (called "Type A") suffered coronary heart disease at a rate three times as great as "Type B" men, who were characterized by an absence of some or all of these competitive drives.

The study concerning municipal drinking water is by Henry A. Schroeder, M.D., of the Dartmouth Medical School, Hanover, N.H., and Brattleboro Memorial Hospital, Brattleboro, Vt.

Dr. Schroeder found significant differences in the bulk and trace constituents of water from the 25 U.S. cities with the highest and the 25 cities with the lowest death rates from arteriosclerotic heart disease.

The water associated with high death rates had less "hardness," magnesium, sodium, potassium, sulfate, and barium and more copper. The higher the death rate, the greater were the concentrations of copper and possibly manganese in water.

Dr. Schroeder emphasizes that the study measures municipal water supplies, not water as it comes from the tap after running through pipes and lines. Soft water is notably corrosive in pipes, and material from this corrosion may also be a factor in heart disease, he pointed out.

"The data from the United States, Great Britain, Sweden, and Japan suggest that some quality of water may influence cardiovascular death rates," Dr. Schroeder said. "The waters associated with the highest death rates in all four areas were of a nature considered corrosive to metal pipes."

If the relationship between softness of water and coronary heart disease is valid, he said, two hypotheses must be explored: (1) Some substance dissolved in water partly protects against or retards heart disease or (2) Some quality in water enhances the disease.

In the study of coronary heart disease risk, researchers noted that behavior pattern was the

(Continued on Page 44)



She's on a diet.  
She's discouraged.  
She needs your help.

You can encourage her  
with DEXAMYL®

brand of dextroamphetamine  
sulfate and amobarbital

'Dexamyl' is the mood-lifting  
anorectic; it not only assures  
unexcelled control of appetite  
but also improves outlook.

*Formula:* Each 'Dexamyl' Spansule® (brand of sustained release capsule) No. 1 contains 10 mg. of Dexedrine® (brand of dextroamphetamine sulfate) and 1 gr. of amobarbital, derivative of barbituric acid [Warning, may be habit forming]. Each 'Dexamyl' Spansule capsule No. 2 contains 15 mg. of Dexedrine (brand of dextroamphetamine sulfate) and 1½ gr. of amobarbital [Warning, may be habit forming].

*Principal cautions and side effects:* Use with caution in patients hypersensitive to sympathomimetics or barbiturates and in coronary or cardiovascular disease or severe hypertension. Insomnia, excitability and increased motor activity are infrequent and ordinarily mild. *Before prescribing, see SK&F product Prescribing Information. Smith Kline & French Laboratories, Philadelphia* **SK&F**





**...but doctor,  
I eat like a bird!**



## IN WEIGHT CONTROL **OBETROL®**

Each OBETROL-10 tablet contains: Methamphetamine Saccharate 2.5 mg., Methamphetamine Hydrochloride 2.5 mg., Amphetamine Sulfate 2.5 mg., Dextro-amphetamine Sulfate 2.5 mg. (OBETROL-20 tablets contain twice this potency) Pat. #2748052.

**INDICATIONS:** This combination of amphetamines may be useful as an adjunct in the management of certain forms of obesity where an appetite depressant is indicated.

**CONTRAINDICATIONS:** Hypertension, advanced arteriosclerosis, coronary artery disease, cardiac arrhythmias, peripheral vascular disease, states of undue restlessness, anxiety, excitement, agitated depression, hyperthyroidism, idiosyncrasy to amphetamine, concomitant administration of a monoamine oxidase inhibitor.

**SIDE EFFECTS:** The most common side effects attended with the use of amphetamines include nervousness, excitability, euphoria, insomnia, dryness of mouth, nausea, vertigo, constipation, and headache.

**DOSAGE:** Initial adult dose is one-half to one 'Obetrol-10' tablet daily, preferably one-half to one hour before meals. This may be gradually increased to one 'Obetrol-10' or 'Obetrol-20' tablet, one to three times daily as indicated.

**SUPPLIED:** In bottles of 100, 500, and 1,000 scored tablets.

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## Two Reports On Heart Disease

(Continued from Page 42)

most significant factor in anticipating heart disease among previously healthy men.

After 2½ years of observation, 70 of the 3,182 men studied had suffered coronary heart disease. The rates were 4.8 cases per 1,000 among men aged 39 to 49, and 18.6 per 1,000 among those aged 50 to 59 at the beginning of the study.

Eighty-five per cent of the younger men who suffered heart disease were the active, "Type A" men. Seventy-two per cent of the older men were in this category.

Men who had heart disease appeared to earn more; fewer had never smoked, and they exercised less than others in the group, the authors said.

Authors of the study are Ray H. Rosenman, M.D., Meyer Friedman, M.D., and Harley B. Messinger, M.D., Ph.D., of the Harold Brunn Institute, Mount Zion Hospital and Medical Center, San Francisco; Reuben Straus, M.D., and Moses Wurm, M.D., of St. Joseph Hospital, Burbank, and C. David Jenkins, Ph.D., of the School of Public Health, University of North Carolina, Chapel Hill.

## Policy Statement on Population Control Issued by the AMA

The American Medical Association moved in 1965 to implement its first statement on population control since 1938. In late 1964 the AMA House of Delegates adopted a position that "the prescription of child-spacing measures should be made available to all patients who require them, consistent with their creed and mores, whether they obtain their medical care through private physicians or tax or community-supported health services."

The previous AMA statement said such measures should be given "only in dispensaries, clinics and similar establishments licensed to treat the sick and under medical control."

The new policy statement says that the subject of reproduction and birth control is a matter of responsible medical practice as well as responsible parenthood. It urges the medical profession to accept a major responsibility in matters related to human reproduction as they affect the total population and the individual family. Doctors are told they must be prepared to provide adequate counsel and guidance when the needs of the patient require it. A manifestation of the new policy appeared in the *Journal of the American Medical Association* in October 1965, in the form of a medical evaluation of all known contraceptive methods. Prepared by physicians and adopted by the AMA Committee on Human Reproduction, the evaluation of contraceptive methods was designed to aid the physician in patient counseling.



# Now...“Instant Air” and “Constant Air” for your Asthmatic Patients



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Dilabron® (brand of isoetharine)  
methanesulfonate 0.6%  
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Thenyldiamine HCl 0.05%

2. Tablets give “constant air”  
for routine maintenance

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Each tablet contains ephedrine sulfate 24 mg;  
glyceryl guaiacolate 100 mg; theophylline 100 mg;  
phenobarbital 8 mg (warning—may be  
habit-forming); and thenyldiamine HCl 10 mg.

### Combined

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### Therapy...

- expands vital capacity
- stabilizes the asthmatic patient
- offers minimal side effects and reduces chance of drug resistance
- frees lungs of trapped air and mucus
- reduces the need for emergency parenteral therapy

Prescribing information: BRONKOTABS: 1 tablet every 3 or 4 hours, not to exceed 5 times daily. Children over 6: one half adult dose. BRONKOMETER: Ready to use 10 ml pocket aerosol. Delivers at mouthpiece 200 metered doses of 350 mcg Dilabron® (brand of isoetharine) methanesulfonate; 70 mcg phenylephrine HCl; 30 mcg thenyldiamine HCl with saccharine and menthol, and fluorochlorohydrocarbons as inert propellants. Preserved with ascorbic acid 0.1% and alcohol 30%. RECOMMENDED DOSAGE: 1 or 2 inhalations with at least 1 minute between inhalations. Occasionally more may be required. In most cases, inhalations need not be repeated more often than every 4 hours.

PRECAUTIONS: Bronkotabs Sympathomimetic side effects are minimal and there are none of the problems associated with steroid therapy. However, frequent or prolonged use may cause nervousness, restlessness or sleeplessness or other usual sympathomimetic side effects. Bronkometer Same precautions as for Bronkotabs. In addition, Bronkometer should not be administered simultaneously with epinephrine or similar compounds because of the possibility of tachycardia, but it may be alternated with these agents. Dosage of Bronkotabs and Bronkometer must be carefully adjusted in patients with hyperthyroidism, diabetes, hypertension, acute coronary disease, cardiac asthma, and limited cardiac reserve, and individuals sensitive to sympathomimetic amines.



BREON LABORATORIES INC., 90 Park Avenue, New York, N.Y. 10016

## Neurological Science Meeting Slated for San Francisco in March

The Federation of Western Societies of Neurological Science will hold its Second Annual Meeting in the Hilton Hotel, San Francisco, March 3, 4, 5, 6, 1966. This meeting will feature a variety of presentations on basic and clinical neurology. In addition there will be a symposium on epilepsy and a symposium on neurochemistry. These symposia will have presentations by investigators prominent in these fields from all over the United States. Dr. Earl Walker and Dr. Preston Robb will contribute to the symposium on epilepsy.

The Program Director for this meeting is Dr. Robert Aird of San Francisco. The Federation was formed by the San Francisco Neurological Society, Puget Sound Neurological Group, Southern California Neurosurgical Society, Los Angeles Society of Neurology & Psychiatry, and the San Diego Academy of Neurosurgery.

For further information please write:

HOWARD S. BARROWS, M.D., *Chairman*  
Federation of Western Societies of  
Neurological Science  
1200 North State Street, Box 93  
Los Angeles, California 90033

## Ten Large Grants Announced for Cedars-Sinai Medical Research

Ten research grants totaling \$379,537 have been awarded to investigators at the Cedars-Sinai Medical Research Institute by the National Institutes of Health of the U.S. Public Health Service.

The researchers and their approved projects are:

Mr. Morton Maxwell, "Kinetics of Peritoneal Dialysis," a study of the rate at which certain substances can be removed from the body through dialysis of the peritoneal cavity.

Dr. Nancy Warner, "Pathology of Pancreatic Circulation," a study of abnormal blood circulation within the pancreas.

Dr. Raymond Caren, "Pancreatic Alpha Cell Function and Lipid Metabolism," an investigation of the enzymes produced by the pancreas and their effect on the formation of fats which can be significant in some diseases of the heart.

Dr. William Stone, "Surgical Polymers—Standardization and Synthesis," an effort to create an artificial cornea, and "Anterior Chamber Drainage Tubes," an attempt to induce artificial drainage of fluid under high pressure from the anterior chamber of the eye to prevent optic nerve damage which can lead to blindness.

Dr. Harold J. C. Swan, "Ventricular Function in the Hypertrophied Heart," a study of the ability of the diseased heart to pump blood.

Dr. Eliot Corday, "Mechanisms of Atrial Flut-

(Continued on Page 52)

# DEPROL®

meprobamate 400 mg. +  
benactyzine hydrochloride 1 mg.

**Indications:** 'Deprol' is useful in the management of depression, both acute (reactive) and chronic. It is particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination. It is also useful for management of depression and associated anxiety accompanying or related to organic illnesses.

**Contraindications:** Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

**Precautions:** *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

**Side effects:** Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

*Benactyzine hydrochloride*—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

*Meprobamate*—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

**Dosage:** Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

**Supplied:** Light-pink, scored tablets, each containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.

Before prescribing, consult package circular.



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CD-5726

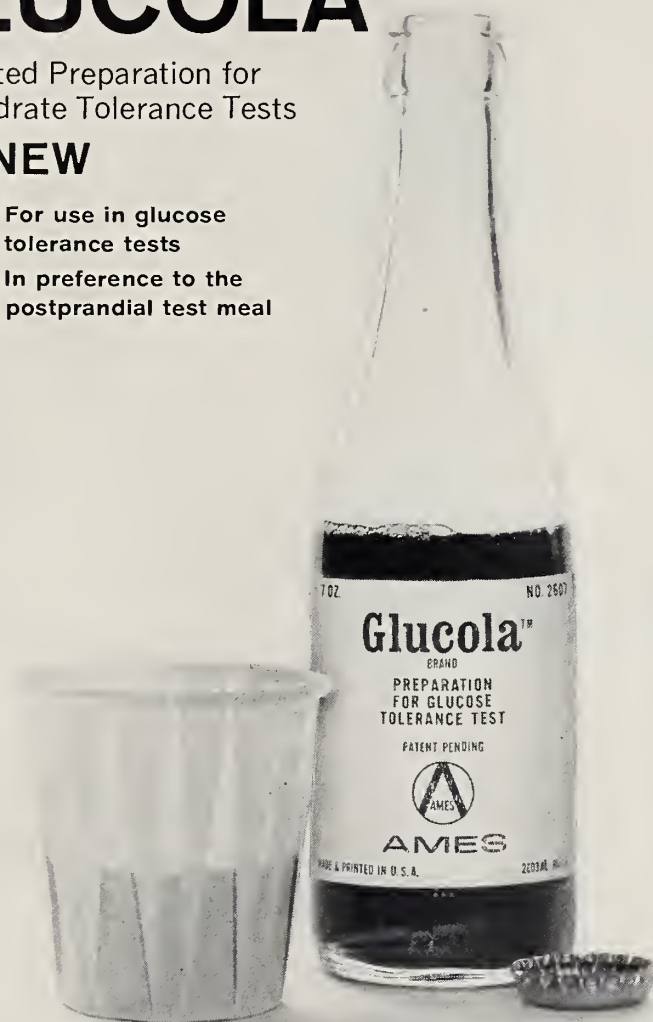


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Ready to use • Pleasant tasting cola flavor • Well tolerated

A 7-ounce bottle of GLUCOLA provides a liquid oral loading dose equivalent to 75 Gm. of glucose\* for carbohydrate tolerance testing. GLUCOLA avoids the nausea that frequently results from lingering sweet laboratory preparations, and the occasional emesis that necessitates rescheduling the test. With GLUCOLA, no time is lost weighing and mixing glucose "cocktails"—only a bottle opener is needed.

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## Ten Large Grants Announced for Cedars-Sinai Medical Research

(Continued from Page 46)

ter and Fibrillation." Abnormal heart rhythms begin in the atrium, the upper chambers of the heart, and Dr. Corday is trying to find out how and why.

Dr. Joseph Katz, "Glucose and Propionate Metabolism," a study of the body's ability to assimilate sugars and fats.

Dr. Charles Kleeman, "Homeostatic Regulation in Chronic Renal Disease," a study of the function of normal regulatory mechanisms in chronic kidney disease, and "Experimental Adrenal Insufficiency," experimental work involving malfunction of the adrenal gland.

### Benefit vs. Risk That Is the Ratio

Since there is no such thing as an absolutely safe drug, nor is there a drug that will prove effective in every patient in which it is used, the best we can achieve is a balance; that is, where potential benefit outweighs potential risk. It should be stressed that the benefit-risk ratio is not a constant. The scientist can afford a larger risk in a severe disease for which there is no completely effective therapy, for example, in leukemia, than he can in a relatively benign disorder. FDA Commissioner George P. Larrick in *Emory University Quarterly* (21:95), Summer 1965.

### AMA Health Information Widely Distributed

More than 31 million pieces of literature, mostly related to health information and education, have been distributed by the American Medical Association so far this year.

This is more than twice the amount distributed in 1964, the AMA said.

Steadily increasing requests indicate that AMA literature plays a significant role in schools, conferences, health improvement efforts, careers days, and for individual information, said F. J. L. Blasingame, M.D., AMA executive vice president.

Some of the more popular items:

An emergency medical identification card, a family health record, and the pamphlets, "Until Your Physician Comes," "Smoking: Facts You Should Know," and "First Aid Manual."

Approximately 50,000 orders for a sex education pamphlet arrived after it was mentioned by a nationally syndicated columnist.

More than 80 pamphlets and two sets of 12 full-color posters are available from the AMA. A small charge is made to defray costs of mailing and printing some items. For a list of publications, write to the Circulation and Records Department, American Medical Association, 535 N. Dearborn St., Chicago, Ill. 60610.



# Report to Doctors

## **The sip-and-run breakfast**

How many of your patients start the day with a sip of coffee, half a doughnut, and a fast run for the bus? The purpose of the ad on the left is to alert such people (and there are millions of them) to the folly of careless nutrition habits. It will appear in LOOK, LIFE, TIME and SUNSET.\* We hope you will read this advance proof before your patients have a chance to do so. Probably, you will find it reinforces many things you have often pointed out. This is one of a series of advertisements whose object is simply this: To help you improve family health by increasing their understanding of nutrition.

\*The references to Food Groups and to specific amounts of food in this advertisement are those recommended by the Food and Nutrition Board of the National Research Council. Reference material and patient aids concerning proper food selection will be sent to you upon request. Write the Dairy Council of California, Box 2066C, Sacramento.

# Your Heart Fund Fights

HEART ATTACK • STROKE  
HIGH BLOOD PRESSURE  
INBORN HEART DEFECTS



## Openings in General Medicine and Psychiatry in State hospitals and youth and adult correctional facilities

Although most vacancies are in the field of psychiatry, there are frequent openings in general medicine in State facilities. These offer opportunity to develop psychiatric skills if interested.

Because of the wide variety in medical and rehabilitation activities in both mental health and correctional institutions, many doctors can broaden their experience in State service, and enter for that reason. Your inquiry is invited.

Write for details to: William F. Webster  
State Personnel Board  
Sacramento, California 95814

## Drugs and Driving

(Continued from Page 12)

treat a variety of functional states, and effects of these drugs on the autonomic nervous system are widespread," the authors said.

The patient's ability as a driver is a major factor in determining his drug dosage. But it may not always be easy to evaluate these abilities, the article pointed out.

"A patient's inability to resist impulses may be reflected in an urge to pass another car at a dangerous moment; he will be subject to even further loss of judgment when he is taking such drugs as meprobamate, amphetamine, or phenobarbital," the article said.

Accident-prone persons may be more susceptible to the side effects of medication. "Such persons should be cautioned against driving while taking drugs, no matter how safe the drugs might ordinarily be," said the article.

The special problem of alcohol is that both legal and social sanctions against driving under the influence of alcohol are comparatively weak, the authors said. They cited the stringent laws of Scandinavia and the acceptance by its citizens that "if you drink anything alcoholic you should not drive that day."

Another delicate problem the doctor faces is that his very cautioning words may destroy some of the intended therapeutic effect of the drug.

In this situation, the patient should be told about the expected benefits of medication and that if other effects occur, he should call his physician before deciding whether to drive.

If a drug "carries even a slight hazard, and if the patient has no practical or emotional need to drive, the physician can easily advise against driving. However, such a situation must be rare in present-day American society since almost everyone can claim a practical need to drive," the authors said.

Adolescents and young adults "are especially sensitive to the loss of driving privileges," they said. "Their feelings illustrate the almost universal emotionalism concerning cars."

Using these guidelines, the use of alcohol probably is the only instance in which the driving privilege should be categorically denied, the authors said.

"Physicians do not want to act as enforcers of social policy, but by assuming the responsibility of educating their patients about drugs and driving safety, they can serve the patient and the community in a realistic way," the authors said.

The article appeared in the January 31 issue of *JAMA*.

VISIT SCIENTIFIC AND  
TECHNICAL EXHIBITS  
C.M.A. 1966 ANNUAL SESSION



## Drug Abuse Regulations Became Effective February 1, AMA Reminds Physicians

The Drug Abuse Control Amendments of 1965, establishing special federal controls for depressant and stimulant drugs, went into effect on February 1 this year.

The American Medical Association reminds physicians that they should be prepared to practice under the law.

The amendments provide for regulation of the manufacture, distribution, delivery and possession of depressant and stimulant drugs. Under the law these include barbiturates, amphetamines, and other drugs which have a potential for abuse because of their depressant or stimulant effect on the central nervous system or because of their hallucinogenic effect. Not covered in the amendments are narcotic drugs—opium, morphine, heroin, marijuana, etc.—which are regulated under another statute.

Physicians are covered by the law as well as drug manufacturers and processors and their suppliers, wholesale druggists, licensed pharmacists, hospitals, clinics, public health agencies, research laboratories and educational institutions who use the drugs in research, teaching or clinical analysis but do not sell them. Under the law no other persons or organizations may legally handle the drugs.

Provisions of the law that involve physicians:

—All persons, including most physicians, who handle depressant and stimulant drugs defined in the law must prepare a complete and accurate inventory of their stocks on hand as of February 1, 1966. This record must be kept for at least three years.

—From February 1 onward, a record must be kept of all depressant and stimulant drugs received and dispensed. This applies chiefly to pharmacists, but also applies to most physicians who receive and dispense drugs, including professional samples. In the record must be included: for stimulant and depressant drugs received—the kind and quantity of the drug, the name, address and Food and Drug Administration registration number of the person from whom it was received, and the date of the transaction; for stimulant and depressant drugs dispensed—the kind and quantity of the drug dispensed or otherwise disposed of, the name and address of the person obtaining the drug, and the date of the transaction. The records must be kept for three years unless state laws specify a longer period. In most instances the wholesaler or manufacturer invoice will be adequate for a receipt record, provided the necessary information is included.

—All records must be open to inspection at

(Continued on Page 27)

## A movie for physicians and dentists only.

Would you like your billing problems reduced to one simple daily procedure? See Bank of America's new 7½ minute film "Professional Billing Service". A bank representative will call at your office without obligation, show you the movie—and explain how this computerized service can save you time and money. Just fill in coupon and mail to:

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*common cold! I thought everything was a "virus" these days.*

ough he'd prefer a more exotic name for it, you know suffering from an ordinary, old common cold. And, congested. He'll breathe easier when you prescribe Novahistine LP.

long-acting tablets in the morning and two in the evening will provide around-the-clock relief by helping keep congested air passages clear, thus enabling the cold patient to enjoy normal and free breathing. The action of long-acting Novahistine LP helps restore normal mucus secretion and ciliary activity—physiologic defenses against infection of the respiratory tract.

cautiously in individuals with severe hypertension,

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Each Novahistine LP tablet contains: phenylephrine hydrochloride, 25 mg., and chlorpheniramine maleate, 4 mg.

# NOVAHISTINE® LP

*For relief of nasal congestion.*



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## Leukemia May Result By Cancer-Causing Viruses

A disease that remains largely cloaked in mystery is human leukemia. More than any other human cancer, viruses seem implicated in its cause and yet proof of a viral etiology is still lacking. Heredity sometimes seems to play a role, too: leukemia is sometimes observed to "run" in families. Viruses are the proven cause of some animal leukemias.

In 1965, for the first time, a cancer-causing agent that may be a virus appeared to have been implicated in the production of human leukemia.

Presumptive evidence of the agent was found

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in a family where an abnormal chromosome (known as the Philadelphia chromosome) was detected in: (1) a grandfather who recently died of chronic myelogenous leukemia; (2) his daughter, and (3) two grandchildren. Neither the daughter nor grandchildren have the disease but chronic myelogenous leukemia is believed to have claimed the lives of the dead man's father, brother, sister and a nephew.

Chromosomes are the X and Y-shaped cellular bodies that carry the genes of heredity. The Philadelphia chromosome, seen only in persons with chronic myelogenous leukemia, is an abnormal body with part of one arm missing.

A nongenetic, transmissible agent—perhaps a virus—may be responsible for the abnormal chromosome in this family, according to the investigator who reported the work, Kurt Hirschhorn, M.D., assistant professor of medicine at New York University Medical Center.

Why does Dr. Hirschhorn believe that a virus or similar agent is operating in this family rather than some genetic factor?

According to his explanation:

Chromosome analyses were made of members of the family after the high familial incidence of chronic myelogenous leukemia was noted by Leo Weiner, M.D., Bronx Veterans Administration Hospital. Virtually all of the white blood cells in the grandfather's bone marrow (where blood cells are produced) carried the Philadelphia chromosome although the abnormal chromosome was absent in other cells. In the healthy daughter and two healthy grandchildren the Philadelphia chromosome was found in only 10 to 15 per cent of the white blood cells—a percentage one would not expect to find if development of the Philadelphia chromosome was genetically determined.

What appears to have been transmitted from parent to offspring was a nongenetic tendency for the abnormal chromosome to occur. Dr. Hirschhorn pointed out that: (1) the Philadelphia abnormality is apparently caused by deletion of one arm of the chromosome, and certain viruses are known to cause chromosomal aberrations in tissue culture; and, (2) transmission of leukemia virus is known to occur between female mice and their offspring.

Whether the healthy daughter and grandchildren will eventually develop chronic myelogenous leukemia is a question that will be answered only with time—perhaps 30 years—since the disease characteristically has a late onset. Whether or not the disease develops, said Dr. Hirschhorn, may depend upon the ability of each person's body to maintain an internal environment hostile to cells containing the abnormal chromosome.

VISIT SCIENTIFIC AND TECHNICAL EXHIBITS  
C.M.A. 1966 ANNUAL SESSION



## Drug Abuse Regulations Became Effective February 1, AMA Reminds Physicians

(Continued from Page 17)

all times by properly identified Food and Drug Administration inspectors if the physician is dispensing for a fee. If the physician dispenses occasionally for no fee, he should probably have records to prove that no fee is charged.

—Prescription orders must contain the name and address of the patient and date of issue. A prescription order does not, however, have to be signed by the prescriber; the physician may give the prescription order by telephone or direct oral instructions.

—No prescription order can be renewed more than five times, and no prescription order can be dispensed or renewed more than six months after the date of issue. After the five renewals or six months, the physician may give additional authorization for refilling the order. These requirements apply to all prescriptions, regardless of the date of issue.

Penalties for failure to comply with the Drug Abuse Control Amendments of 1965 include both fine and imprisonment.

### Communities Search for Physicians

Thirty-six small communities in 21 states have built or are building two-doctor medical centers under the American Medical Association-Sears Roebuck Foundation Community Medical Assistance Program, and are searching for physicians. Nine other communities are seeking additional doctors, according to the *American Medical Association News*.

Full information is available by writing to Norman H. Davis, secretary, Medical Advisory Board, Sears Roebuck Foundation, 3333 Arthington Street, Chicago, Illinois 60607.

Communities looking for one or more doctors are:

Colorado: Springfield and Oak Creek; Illinois: Gardner, Kirkland, Elizabeth, London Mills, Hartford-Alton, Sheridan and Martinsville; Arkansas: Rector; Iowa: Bedford, Melcher-Dallas, Coon Rapids and Hubbard; Kansas: Waterville; Minnesota: Eveleth, Stephen, Lambertown and Atwater.

Nebraska: Clay Center and Wisner; New York: Bridgeport, North Rose and Arcade; North Carolina: Locust, Newport-by-the-Sea and Bayboro; Pennsylvania: Linesville, Jonestown and Boswell; Virginia: Nickelsville; Massachusetts: Outer Cape Cod; Maryland: Hurlock; Texas: Claude; Missouri: Illmo, Monroe City and Clarkville; Wisconsin: La Farge; Washington: Granite Falls; Indiana: Walton; Montana: Huntley-Worden; Georgia: Glenwood; Nevada: Wells; North Dakota: Glen Ullen.



**...but doctor,  
I eat like a bird!**

## IN WEIGHT CONTROL **OBETROL**

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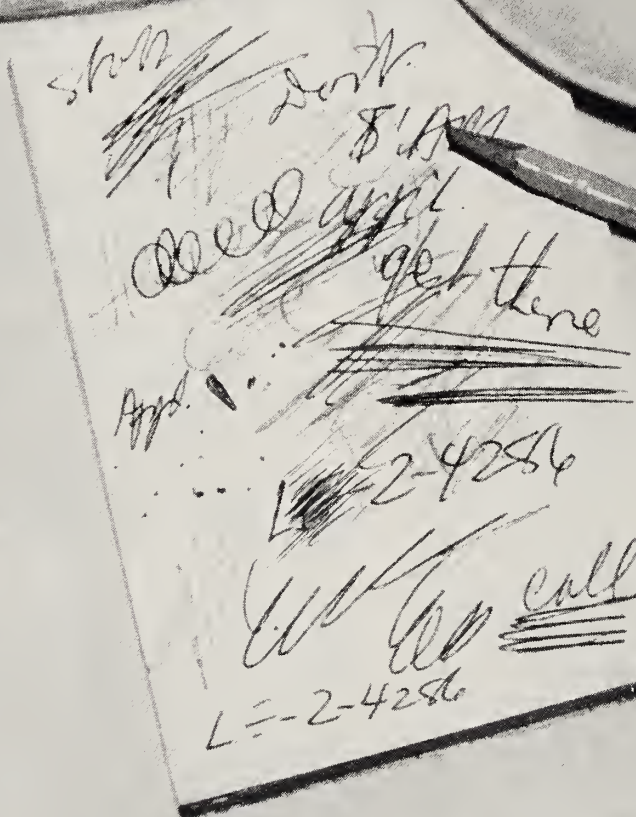
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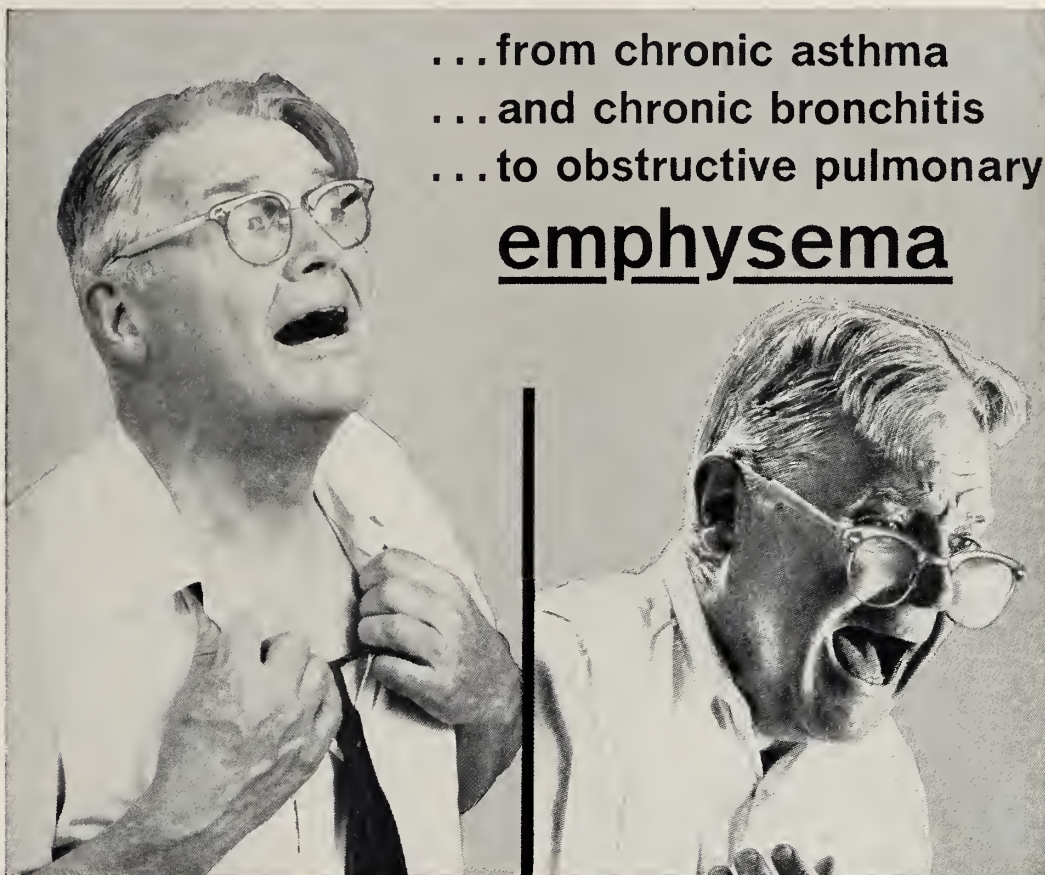
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1. Boren, H. G.: M. Clin. North America 43:48 (Jan.) 1959.

2. Jackson, R. H., et al.: Dis. Chest 45:75-85 (Jan.) 1964.

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## The Performance of Professors

The more uric acid in your blood, the more likely that you are an outstanding performer in your job.

Your amount of drive, achievement, and leadership may be positively associated with the level of uric acid in your blood serum, according to a report in the February 7 *Journal of the American Medical Association*.

Uric acid is a nitrogenous waste product of the body's metabolism.

It hasn't been determined why performance is related to the body's serum urate levels. The two University of Michigan investigators who did the research, however, favor the idea that uric acid acts as a stimulant to the brain.

Their research also lends support to another hypothesis: that "a tendency to gout is a tendency to the executive suite." In other words, the same high levels of uric acid which stimulate performance also help cause the painful inflammation of gout, the "disease of kings."

The report is based on a survey of 113 male faculty members at the University of Michigan. When these men were examined, the authors found a significant relationship between (1) the professors' drive, professional achievements, and leadership qualities, and (2) the serum urate concentrations of their blood.

Blood serum was examined during a voluntary annual physical checkup. The data on the professors' work behavior were gathered by a clinical psychologist in voluntary, two-hour interviews.

The investigators defined "drive" as a measure of an individual's output of energy in daily activities. Men who worked at top speed or with great intensity were found to be among those with the highest concentrations of uric acid.

The rating of "achievement" focused on the man's self-esteem and self-confidence in his work. Again, the professors with highest serum urate levels also had the highest achievement ratings.

The third rating, "leadership," also was related to uric acid levels. This was a measure of the tendency to lead others by persuasion. Strong leaders were considered to be those with an interest in the smooth functioning of personal relationships.

Leaders usually had a "greater interest in manipulating people than things," the authors said.

Other investigators have proposed that persons with high serum urate levels are on the average more intelligent, or at least less susceptible to some kinds of fatigue. The authors, however, said they believe uric acid's effect "has a much stronger relationship to achievement . . . than it has to high scores on intelligence tests."

Pharmacological experiments are now needed,

(Continued on Page 33)

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**Precautions:** *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

**Side effects:** Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

*Benactyzine hydrochloride*—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

*Meprobamate*—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

**Dosage:** Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

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## The Performance of Professors

(Continued from Page 30)

they said, to determine if the concept of serum urate as a stimulant can be supported.

The authors are George W. Brooks, M.P.H., and Ernst Mueller, Ph.D., of the Institute for Social Research and the Mental Health Research Institute, University of Michigan, Ann Arbor.

### Will Palm-Reading Detect Cancer?

It's possible that a bit of medical palm-reading may reveal the presence of cancer.

This was suggested when three staff members at the University of Oregon Medical School noticed a frequent characteristic of cancer patients: many had small, horny growths on the palms of their hands.

These growths, called keratoses, were found four to five times as frequently in persons with cancerous tumors as in a comparable group without cancer, the investigators report in the November *Archives of Dermatology*, published by the American Medical Association.

The small growths are *not* an absolute indication that a person has cancer, the article points out. The keratoses also were found in about 7 per cent of a study group of 685 patients who did not have cancer.

However, in a group of 671 patients with several types of cancerous tumors, 218, or 32 per cent, were found to have the growths on their palms.

The keratoses are circular, and so small they frequently go unnoticed. They usually are pearly white, flesh-colored, or yellow. Their dim appearance can sometimes be made clearer by rubbing water or alcohol on the palm, the author said.

There was another finding: the growths resemble those caused by arsenic, and 13 per cent of the cancer patients and 10 per cent of the control group had had exposure to arsenic in one way or another. Arsenic is known to be a cancer-causing agent.

It's not logical at this time, however, to assume that either the palm growths or the patients' tumors were caused by arsenic, the authors cautioned. More needs to be known about the relationship of these keratoses to cancer.

Regardless of cause, "the presence of palmar keratoses should be regarded as a suggestive sign of cancer and should be diligently searched for in all patients," the authors said.

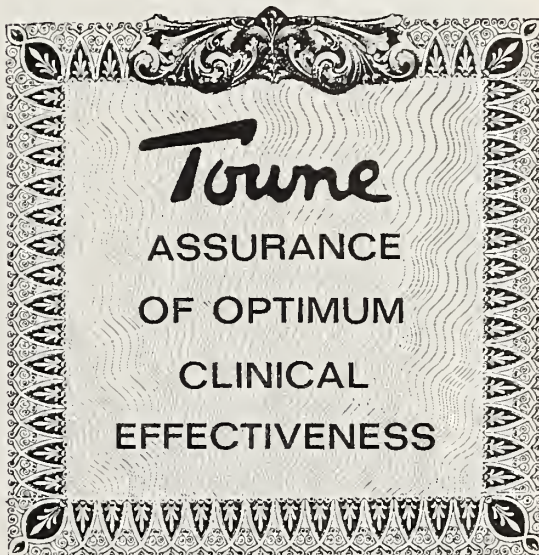
The authors said they didn't know whether the palm growths have any value as a screening test for cancer, but they are starting investigations to find out.

The authors are Richard L. Dobson, M.D., Marvin R. Young, M.D., and Jeffery S. Pinto, M.A., of the Division of Dermatology of the University of Oregon Medical School, Portland.



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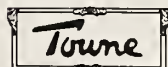


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# Etiology of Leukemia

## A Review

A. WILLIAM SHAFER, M.D., *La Jolla*

■ *A variety of factors probably are etiologically involved in leukemia, not only in different cases but also within individual cases.*

*Abnormalities of chromosomes have been found in various types of leukemia. Whether these chromosomal alterations are primary or secondary is undetermined, but it is likely that they are at least contributory in the development of leukemia. There is an increasing body of evidence incriminating viruses in leukemogenesis in man, and they may be a factor in all cases. Certain chemicals may be important etiologic factors in a few cases. Many different studies have established that ionizing radiation in large doses may be leukemogenic. Whether small doses of irradiation are dangerous has not been demonstrated.*

IN THE LAST TWO DECADES great strides have been made not only in the treatment of leukemia but also in the study of the etiology of this neoplastic process and of the abnormal metabolic processes in leukemic cells.

At present the evidence suggests that a number of various causative factors may be operative in leukemia in different cases. Indeed, it seems very likely not only that there are multiple factors involved in different cases, but that the same is true in individual cases. Some of the evidence implicating alteration of nucleic acids, viruses, chemical factors and irradiation in leukemogenesis will be discussed.

### Nucleic Acids and Chromosomes

It is now recognized that deoxyribonucleic acid (DNA) in chromosomes performs two important control functions. First it controls cell division because of the necessity for it to replicate itself for mitosis to occur, and second it determines nucleotide sequence in ribonucleic acid which in turn determines amino acid sequence in proteins. Therefore, in uncontrolled proliferation of cells as seen in leukemia these functions of DNA would be expected to be faulty. If so, the chromosomes might be morphologically abnormal, although not necessarily so. Since 1960, a number of chromosomal abnormalities have been found in the various types of leukemia.

Nowell and Hungerford<sup>41</sup> in 1960 first reported an abnormality of chromosome 21 in chronic

Head, Division of Hematology, Scripps Clinic and Research Foundation, La Jolla.

Prepared at the request of the Committee on Scientific Information of the Scientific Board, California Medical Association.

Submitted 24 May 1965.

granulocytic leukemia (CGL). This abnormal chromosome, called Philadelphia chromosome or Ph<sup>1</sup>, is characterized by the absence of a part of one of its long arms. When bone marrow is examined directly, the majority of dividing cells in most cases of CGL have been Ph<sup>1</sup> positive irrespective of the stage of the disease and of therapy. There is good evidence that the Ph<sup>1</sup> chromosome is present not only in the granulocytic but also in erythrocytic precursors and megakaryocytes.<sup>22,53</sup> Kraus, Sokel and Sandburg<sup>35</sup> classified CGL into two groups on the basis of the presence or absence of Ph<sup>1</sup>. In the Ph<sup>1</sup>-positive group were typical cases of CGL, whereas in the Ph<sup>1</sup>-negative group the patients tended to be older men in whom the hematologic features were unusual and difficult to classify and who responded poorly to therapy. A single case of Ph<sup>1</sup>-negative CGL in which the patient responded poorly to therapy was also reported by Crawford and Pegrum.<sup>15</sup> At this time it is fair to say that diagnostically if the Ph<sup>1</sup> chromosome is present, the patient has CGL; if Ph<sup>1</sup> is absent, the patient may have CGL although this must be rare<sup>48</sup>; and that the absence of Ph<sup>1</sup> may be helpful prognostically in CGL.

In 1962 Gunz and Fitzgerald<sup>25</sup> reported an abnormality of the short arm of a small acrocentric chromosome (probably 21) in several members of a family in which there were two cases of chronic lymphocytic leukemia (CLL). More recently Court Brown<sup>12</sup> and Heni and Siebner<sup>31</sup> each studied a family in which there was more than one case of CLL, and no abnormalities of the chromosomes were found.

Various chromosomal abnormalities, both in structure and in number, have been found in acute leukemia.<sup>‡</sup> The changes have been unique in each case, and it has not been possible to correlate the changes with any clinical picture. In individual cases, however, the abnormalities have been consistent irrespective of the stage of the disease or the response to therapy.<sup>21</sup>

The significance of these chromosomal abnormalities in leukemia remains to be determined, but it seems likely that they are either primary and causal or at least secondary but contributory.<sup>26</sup>

## Viruses

In 1951 Gross<sup>23</sup> reported that leukemia developed in a strain of mice in which spontaneous

leukemia does not occur (C3H strain) after the injection of cell-free extracts of leukemic tissue from a strain of mice in which leukemia had developed spontaneously (AK STRAIN). He also was able to produce leukemia in the C3H mouse by injecting an extract made from embryos of non-leukemic AK mice. Feldman and Gross<sup>20</sup> subsequently demonstrated by electron microscopy the presence of virus-like particles in several organs of C3H mice with this induced leukemia.

In spite of unsuccessful attempts to transmit leukemia from man to man,<sup>50</sup> in the last few years an increasing body of evidence has accumulated suggesting an etiological relationship between viruses and human leukemia. Almeida and coworkers<sup>2</sup> consistently found virus-like particles in the blood of two patients with acute granulocytic leukemia. Dmochowski<sup>18</sup> has reported the presence of virus particles in the lymph nodes of the majority of patients with various types of leukemia and lymphoma. These particles morphologically were similar to those found in mouse, rat and chicken leukemia. Whitaker and coworkers<sup>54</sup> were able to produce cellular alterations in cells in tissue culture when they were inoculated with cell-free extracts of human leukemic brain; whereas extracts from normal human brain did not produce similar changes. In 1964 Negroni<sup>40</sup> reported that a cytopathic virus was cultured from the bone marrow of 40 per cent of patients who had leukemia. Antisera to these viruses neutralized 100 tissue culture doses of the homologous strain. Negroni also found that in seven of eight patients with leukemia a 1:10 dilution of their serum neutralized between 10 and 100 tissue culture doses of this virus. Herpes simplex antisera did not kill these viruses. More recently Murphy, Furtado and Plata<sup>39</sup> isolated cytopathic agents from the bone marrow of 45 per cent of children with acute leukemia. Virus-like particles were seen on electron microscopy of the infected tissue culture cells; and the agents isolated, when injected into mice, produced a leukemia-like picture.

There have been several reports of clustering of cases of leukemia. In Niles, Ill., where eight cases of acute leukemia occurred in children in a three-year period,<sup>29,30</sup> all but one of these children either attended or had a sibling attending the same school. Other instances of clustering of leukemia have been reported.<sup>43,49</sup> Evidence against the occurrence of clusters by mere chance has been reported by Ederer.<sup>19</sup> Schwartz and cowork-

‡Reference Nos. 11, 21, 32, 34, 38, 44, 52.



ers<sup>45</sup> examined specimens of serum from the other members of the families of the patients with leukemia in the Niles cluster. Using brain tissue from patients with leukemia as an antigen, they were able to demonstrate an antibody in over 40 per cent of the specimens. They also found positive reactions in specimens of serum taken from 12 of their laboratory personnel working with experimental leukemia—including four who had negative reaction\* when they first began this work. These studies of leukemia clusters suggest that a specific leukemogen was operative in these cases, and the studies of Schwartz suggest that a virus may have been the leukemogenic agent.

### Chemicals

Of all the chemicals to which people in our society are exposed only benzene is widely accepted as a definite leukemogen.<sup>16</sup> However, other chemicals have been implicated—for example, an insecticide, hexachlorocyclohexane.<sup>33</sup>

Various hematologic disorders of obscure cause (such as aplastic anemia) may be followed by acute leukemia.<sup>4,17</sup> Therefore, any chemical or drug which may cause aplastic anemia, for example, should be held suspect as a possible leukemogenic agent. There is a good deal of circumstantial evidence to implicate phenylbutazone in this regard. In 1960 Bean<sup>3</sup> reported three or four cases of acute leukemia in elderly persons who had been receiving this drug. Subsequently, single cases of acute leukemia following the administration of phenylbutazone were reported by at least six observers.<sup>7-10,28,51</sup> In 1964 Woodliff and Dougan<sup>55</sup> reported five cases in which there was this association. They estimated that in western Australia, during the period of their study, in 9 per cent of the cases of acute leukemia phenylbutazone had been given previously. If there is an increased incidence of leukemia among those receiving phenylbutazone, those most likely to be affected are elderly patients who have taken the drug for long periods and who have had bone marrow depression.

### Radiation

It has been recognized for many years that radiation may be leukemogenic, and many different studies have supported this belief. Abbatt and Lea<sup>1</sup> collected reports of cases of ankylosing spondylitis in England, and did not find leukemia in any of 399 males who had not received x-ray

therapy. On the other hand seven cases occurred in 1,627 males who had received x-ray therapy (expected incidence in general population, 0.33 cases). Court Brown and Doll<sup>13</sup> in an extensive study of 13,200 patients with spondylitis who were treated with x-ray found 32 proven and five probable cases of leukemia. Almost all the cases of leukemia occurred in those who had received over 500 r to the spinal column, and there was a linear relation between dose and incidence of leukemia in the mid-dose ranges. An increased incidence of leukemia has been noted also in children who have had x-ray therapy to the thymus.<sup>42,47</sup> Although Court Brown and coworkers<sup>14</sup> found no increase in leukemia in children who had received in-utero radiation, other investigators have reported evidence to the contrary. For example, MacMahon<sup>37</sup> found that mortality from leukemia was 40 per cent higher in children exposed in-utero.

Recent studies of American radiologists have revealed important statistics concerning the long-term effects of radiation exposure. In a study of nearly 50,000 man-years at risk, Lewis<sup>36</sup> found that deaths from leukemia were three times higher than expected. More recently Seltser and Sartwell<sup>46</sup> compared death rates of various medical specialists in the United States. He also found an increased mortality from leukemia in radiologists as compared with other medical specialists.

The greatest body of information concerning radiation leukemogenesis has been collected by the Atomic Bomb Casualty Commission in Japan.<sup>6</sup> The Commission's data reveal an increased incidence of leukemia in the people exposed to more than 50 rad, with a linear relationship between dose and incidence of leukemia in those exposed to between 100 and 500 rad. The increased incidence of leukemia was first seen one year after exposure; the maximum risk was found four to seven years after irradiation; and although the risk subsequently declined, there was still an increased risk as long as 14 years after exposure.

Although there is no question that large doses of radiation can be leukemogenic, it is not known whether there is a similar risk from smaller amounts of irradiation—that is, whether there is a threshold below which there is no danger. No studies to date have revealed evidence of leukemogenesis from diagnostic radiation. Of interest, however, is the report of Bloom and Tjio<sup>5</sup> of chromosomal abnormalities in blood cells of

patients who had received a skin dose of 12 to 35 r from x-ray studies of the gastrointestinal tract. In spite of the lack of positive evidence that diagnostic use of x-ray may be harmful, it is entirely possible that repeated fluoroscopic examination may be leukemogenic. The following from an editorial by Gunz and Atkinson<sup>27</sup> is worth quoting: [It may be that the] "acquisition of radiation leukemia may be among the fringe benefits of some executive positions."

Scripps Clinic and Research Foundation, 476 Prospect Street, La Jolla, California 92037.

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# Fluorescent Treponemal Antibody Tests

## A Summary and Comparison

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■ *A comparison of current serologic tests for syphilis shows that treponemal tests are preferable to reagin tests in detecting specific antibodies, but that reagin tests are best for determining the response to treatment. The newly developed FTA-absorption technique is suggested as a reliable, inexpensive test for treponemal antibodies.*

THE *TREPONEMA pallidum* immobilization (TPI) test has come to be accepted as the standard of comparison for other tests for syphilis. While the TPI test is a valuable aid in differentiating latent syphilis from a biologically false-positive reaction<sup>3,4</sup> it has certain limitations, namely: (1) it fails to distinguish between various treponemal diseases (for example, syphilis, yaws, pinta, bejel); (2) it fails to distinguish between active and past infection; (3) it cannot be used as an index of therapeutic response; (4) it fails to detect early cases; (5) it is costly, technically difficult, and not readily available.

Over the last several years the fluorescent anti-

body technique has been applied to the laboratory diagnosis of syphilis in attempts to overcome some of the limitations of the TPI test. Several modifications of the fluorescent treponemal antibody (FTA) test for syphilis are now in use throughout the country. The published procedures are generally reliable and give reproducible results but in sensitivity and specificity each method differs from the others. This communication summarizes the various fluorescent treponemal antibody procedures and compares them with the Venereal Disease Research Laboratory (VDRL) test, the Reiter protein complement fixation (RPCF) test and the *treponema pallidum* immobilization (TPI) test.

The fluorescent treponemal antibody absorption test (FTA-ABS)<sup>2</sup> is the most recently de-

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veloped and gives results of greater specificity and sensitivity than its predecessors. The superiority of this modification of the FTA tests results from the use of a new reagent which serves to remove serum components which when present limit the specificity of the test. Like the TPI test, the FTA-ABS differentiates syphilis from biological false-positive (BFP) reactions, and itself rarely gives a BFP result.<sup>1</sup>

While the FTA-ABS has the first three of the five limitations listed above for the TPI test, it overcomes the last two. The FTA-ABS is more sensitive than the TPI in detecting treponemal antibody; it becomes reactive in primary syphilis. It can be done simply and quickly but has not been widely used because of problems in the preparation of the reagent used for absorption. New procedures developed in this laboratory have overcome these problems and the test is now available in many local health department laboratories in California.

The FTA-ABS does not distinguish between the various treponematoses nor does it distinguish between active and old treated cases. For following the patient's response to treatment, the VDRL test remains the test of choice because, unlike the specific treponemal tests (the TPI and FTA-ABS), it frequently becomes non-reactive following treatment. Observing a series of titred dilutions of the VDRL test at appropriate intervals following therapy permits its use as an index of therapeutic response.

The accompanying table summarizes and compares the FTA modifications and other modern laboratory tests for syphilis.

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TABLE 1.—Summary and Comparison of Laboratory Tests for Syphilis

Test	Comment	Determines Presence of Specific Treponemal Antibody?	Compared to the TPI Tests		Useful as Index of Therapeutic Response?
			Early Syphilis	Late Syphilis	
TPI	Determines presence of Treponema pallidum immobilizing antibody in patient's serum	yes	Current reference test		no
FTA	Abbreviation for Fluorescent Treponemal Antibody tests. May refer to any of several modifications of the test	yes	Depends on the particular modification used		no
FTA-5	The original FTA test using 1:5 dilution of serum	yes	higher	equal	no
FTA-100	Modification of FTA-5 using 1:100 dilution of serum	yes	higher	lower	no
FTA-200	Modification of FTA-5 using 1:200 dilution of serum	yes	higher	lower	no
FTA-5-200	1:5 and 1:200 serum dilutions tested simultaneously	yes	higher	equal	no
FTA Absorption (FTA-ABS)	Non-specific antibody is first removed; serum then tested at 1:5 dilution	yes	higher	equal	no
VDRL	Venereal Disease Research Laboratory flocculation test using Cardiolipin antigen	no	higher	lower	yes
RPCF (KRP)	Complement fixation test using a protein fraction of the Reiter treponeme	no	higher	lower	no

\*Sensitivity refers to reactivity of the test in the presence of syphilis. Specificity refers to non-reactivity of the test in the absence of syphilis.

# Acutely Suicidal Patients

## Management in General Medical Practice

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■ *Suicidal crises are best understood as late stages in the progressive breakdown of adaptational behavior in emotionally exhausted patients. The premonitory symptoms of suicide include verbal communications, suicide attempts, symptomatic actions, depression, treatment failure, excessive emotional reactions to specific disease states and panic reactions.*

*Of persons who committed suicide, 75 per cent had seen a physician within six months. To recognize and evaluate suicide danger the physician must not be afraid to question the patient directly about his suicidal plans. The average physician encounters half a dozen suicidal patients a year and will have 10 to 12 suicides in his practice during a long career.*

*In treating suicidal patients, the physician should maintain his medical attitude. The patients need emergency medical care including appropriate drugs. Free communication between patient and physician is very important. This may take some extra time. Patients benefit from emergency psychological support and stimulation toward constructive action. Family, friends, and community agencies should be mobilized to aid the patient. For seriously suicidal patients, consultation is recommended and treatment in hospital is advisable.*

"PREVENTION IS A WATCHWORD of modern medicine."<sup>16</sup> This attitude has led in recent years to increasing emphasis on the role of physicians in preventing suicide. Undoubtedly suicide describes a group of actions and events of great variety and complexity, but the focus of this communication is on recognizing, evaluating, and treating suicidal patients in medical practice.

It is based upon shared experiences and discussions with the staff of the Suicide Prevention

Center\* at Los Angeles, especially with Drs. Farberow, Shneidman and Tabachnick, my associates for many years.<sup>9,10</sup> Additional observations and other points of view can be found in articles by Bennett,<sup>1</sup> Mintz,<sup>12</sup> Motto and Greene,<sup>13</sup> Offenkranz,<sup>14</sup> Robins and coworkers,<sup>15</sup> and Vail.<sup>19</sup>

Who are the suicidal patients? How are they defined? Commonly, the term *suicidal* is applied ambiguously not only to actions of self-murder, self-injury, and self-neglect, but also to threats, communications and thoughts about self-destruction. What are the relationships among these different suicidal behaviors?

In California for 1963, medical examiners and coroners certified approximately 2,800 deaths as

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suicide. Suicide was the ninth leading category of death. About 10 per cent of the suicides were old and sick persons, weary after 65 years or more of life. But the great majority of these deaths occurred in young and middle aged persons with great potentialities and responsibilities. For example, in colleges, on ships at sea and in factories, suicide was the third leading cause of death. Families, physicians and the community felt these suicides unnecessary, unreasonable and uniquely tragic. How can they be explained?

In medical practice, suicide is best understood as the final stage of a progressive breakdown of adaptational behavior occurring in an emotionally exhausted patient. Rough analogies may be drawn to states of physiological collapse; for example, in heat stroke or in untreated adrenal insufficiency. In these examples there is a progressive failure of physiological adjustment with the appearance of premonitory symptoms and signs leading to a potentially fatal crisis. Thoughts of suicide, suicide attempts and numerous kinds of suicidal communications are part of the prodromal symptomatology of suicidal crises.<sup>17,18</sup>

Emotional crises occur from time to time in all lives when people face problems that are temporarily beyond their ability to solve. Situations which threaten the continuity of mental, physical and social equilibrium are powerful stressors. Confrontations with death, ill health, loss of love or change in social status are typical examples. The person under stress feels restless, uneasy, painfully tense and unable to adapt. At first, suicide is only one of many possible reactions. He tries solution a, solution b, solution c, solution d and feels no improvement. He thinks of solutions e, f, g, h and i, and imagines no improvement. Finally, he comes to solution s—suicide. He struggles against it, abandons it, tries other thoughts, other actions. Sometimes nothing helps. He loses hope and returns repeatedly to thoughts of suicide. As his thinking grows more distorted, constricted, confused and desperate, he signals his preoccupation with self-destruction by words, actions and symptoms.<sup>4</sup>

### Prodromal Suicidal Clues

There are a number of prodromal clues:

1. *Verbal Communications.* In over half of the suicide deaths, there is a history of previous, spontaneous, suicidal communications. These statements were direct: "I am going to shoot myself."

"I wish I were dead." Or they were indirect: "You would be better off without me." "How do you leave your body to the medical school?" Sometimes such comments are made directly to a physician, but more often the physician receives the information from frightened friends and relatives who want advice on how to respond to these messages. The most significant interpretation of suicidal communications is that they represent "cries for help." As such, they tend to activate intense emotional responses in persons receiving the communications. More often than not the suicidal situation involves several people.

It should be added that many suicidal patients do not express their self-destructive thoughts spontaneously but will do so if they are asked.

2. *Suicide Attempts.* In one third of the suicide deaths, there is a history of previous suicide attempts. These are intentional self-injuries made in an emotional context resembling suicide. Surveys indicate that physicians in California see about eight suicide attempts for every suicide. Approximately 20 per cent of persons who attempt suicide repeat action of this type at least once. About 5 per cent of the attemptors eventually kill themselves. Half of these deaths occur within a year of the previous attempt, sometimes within hours.

Considering the sizable mortality rate, physicians who treat surgical and medical self-injuries should ask about obvious sources of emotional stress as soon as possible after the self-injury. For a limited time the shock of the suicide attempt causes families and individuals to report truthfully about vital conflicts and embarrassing problems that ordinarily are hidden or distorted by half truths. The disinterested, preoccupied or callous physician loses a golden opportunity to bring concealed problems out into the open where they can be dealt with more effectively.

3. *Symptomatic Actions.* Some suicidal persons communicate their plans by actions. One man bought two caskets, one for his wife who had just died. A student gave away his sports equipment, saying, "I won't need this any more." In struggling against suicidal feelings, some persons take daredevil chances, and they may have a series of accidents or near misses. Increased alcohol intake and irregular attendance at work are common. Requests for increasing amounts of strong sedatives and rapid-acting sleep producers are ominous premonitory clues to suicide.

4. *Depression.* This syndrome is of major importance to physicians because of its frequency, serious disability, danger to life—and good response to treatment.<sup>6</sup> Suicide should be considered as a possibility whenever depressive symptoms are reported. The symptoms are physiological, psychological and social. In all areas the ability to enjoy is lost or seriously disrupted.

Physiological symptoms include sleep disorder, especially sleeplessness; appetite disorder, especially loss of appetite; constipation, dry mouth, headaches, other aches and pains; and fatigue. The psychological symptoms include loss of energy, loss of initiative and absence of interest in usual pleasures, such as sex, sports, books and television. The mood is sad and often guilty, with low self-esteem. Patients tend to feel hopeless and helpless. These emotions are experienced as painful and uncomfortable.

Social withdrawal completes the picture. The patient loses interest in social gatherings and other people, although he may try at times to pretend interest. Often physicians or families suggest a vacation. The realization by the patient that he is unable to enjoy a vacation may be the last straw that precipitates a suicidal crisis.

The depressive syndrome tends to have a discreet onset and a limited duration. Older patients usually have had previous depressive episodes. A family history of depression is common.

5. *Treatment Failures.* In medical practice, suicidal crises tend to be associated with treatment failures. For example, Workman's Compensation has paid a number of death claims recently on workers who remained disabled after treatment for back strain, then killed themselves. Suicide reports often allude to vague abdominal pains or causalgias, persisting after numerous surgical operations. Diseases which impair respiration—for example, emphysema or lymphoma of the neck and mediastinum—are more often associated with suicide than are other chronic illnesses.

6. *Excessive Reactions.* Some attention should be directed toward patients who have an excessive emotional preoccupation with some specific condition, such as pregnancy, obesity or cancer. Even if the patient does not have the particular condition, the negative results of medical examinations should be carefully and repeatedly explained to such patients. It is particularly ironic when a suicide note gives "cancer" as the reason for the act but the autopsy shows no signs of the disease.

In suicide histories dread of heart attacks occurs more commonly than actual coronary occlusions.

7. *Panic Reactions.* About 5 per cent of suicides result from sudden blind panic. Examples: A male school teacher charged with homosexuality dived, in handcuffs, under the wheels of a passing truck. An older man, confused and frightened in an unfamiliar hospital room, jumped out of the window. After an automobile accident, while rescuers attended his badly hurt wife, the uninjured husband wandered off and hanged himself.

### Evaluation of Suicidal Potentiality

Persons who are considering suicide as a potential solution to life crises seek out physicians, hoping for answers less extreme than suicide. Seventy-five per cent of suicides had seen a physician within six months of the death. Unfortunately, patients do not ordinarily reveal spontaneously that they are in suicidal crises. This information emerges readily, however, if the physician asks for it, especially if there is a pre-existing patient-physician relationship of confidence and trust. When he notes prodromal clues to suicide, the physician must decide how to proceed.<sup>7</sup>

Usually, the most tactful and informative technique is to approach the suicidal motivation gradually through a series of questions, working from the more general to the more specific. Such a series of questions might be something like this: "How is your life going? How are you feeling in general? How are your spirits—your mental outlook—your hopes?" If the answers indicate low spirits or pessimistic attitudes or much tension or confusion, another series of questions might be something like this: "Do you wish you could be out of it? Would you like sometimes to give up? Ever wish you were dead?"

If the answers to the above are suggestively affirmative, then a third series of questions might be: "Have you thought of ending your life? How close are you now to suicide? How would you do it? What is your plan?"

1. *Suicide Plan.* The most important, single element in evaluating the immediate suicide emergency is the patient's suicide plan, including the proposed method, place and time. If the patient has decided upon a specific, highly lethal method of suicide with an instrument which is readily available to him, there is a serious emergency. Usually, patients will talk to an interested phy-



sician about the details of their suicide plans, although sometimes this information is obtained from friends or relatives. We take it seriously when a patient sets a deadline for his action; for instance, his fiftieth birthday, retirement day or an anniversary. Vague suicide plans are somewhat reassuring, as are plans to use methods of relatively low lethality, such as aspirin ingestion.

Direct denials are usually truthful and can be relied on, at least temporarily. "Yes, I thought of suicide, but I would never do it because of my children." "For me, suicide is impossible because of my religion." "I would leave town first." The exceptions to this rule—that is, patients who dissemble to friendly physicians—are nearly always obvious psychiatric cases, usually with a history of psychiatric hospitalization.

Physicians who hesitate to ask such direct questions about suicide because of possible harmful effects on patients should be reassured by the experience of the staff of the Suicide Prevention Center in Los Angeles. In interviews with 10,000 suicidal patients and reviews of 3,000 suicide deaths, we found no evidence that such questions had ever harmed patients.

2. *Severity of Symptoms.* Danger signals are: Severe agitation with depression; helplessness, combined with a frantic need to do something; hopelessness which gets worse in response to helping efforts from others; confusion; paranoid trends with persecution delusions or homicidal threats. Five per cent of suicidal patients are also potentially homicidal.

3. *Basic Personality.* Suicidal crises vary in emergency force, according to the patient's character. Persons who have led stable, responsible lives generally respond well to treatment and return to their previous levels. Because of the favorable prognosis, such persons should be the objects of extremely zealous suicide prevention efforts. At present about half of the persons who kill themselves are of that order. Sometimes high social position, public prominence or professional success is a barrier between patients and the help they need. Examples are physicians, military leaders and political figures. Many lives would be saved if persons in crises could accept help without stigma.

By contrast, many unstable, immature, addictive, alcoholic and deviant persons are chronically on the edge of self-destruction. These patients benefit less from emergency first aid. They need

consistent firm direction and long-range rehabilitation.

4. *Precipitating Stress.* If the suicidal crises is a reaction to an overwhelming, sudden stress, the patient needs emergency protection and support but may recover rapidly and spontaneously. This is analogous to heat stroke collapse. If the suicidal crises represent an internal decompensation with no special external stress, the patient may need special study and special treatment, presumably by a psychiatrist. This is analogous to a physiological crisis due to adrenal cortical insufficiency.

5. *Resources.* These include physical, financial and interpersonal assets. The willingness and ability of other persons to aid the patient often is the difference between life and death. Some patients are emotionally bankrupt, and this must be taken into account. For example, many alcoholics, after years of self-destructive behavior which has alienated family and friends, "hit bottom" and are highly suicidal.

6. *Special Indicators* include such factors as family history of suicide, recent suicide of a close friend or relative, anniversary of a divorce or of a death in the family, complete social isolation, history of psychiatric treatment, especially recent discharge from a mental hospital, and recent suicide attempt, unrecognized or untreated.

## Management of Suicidal Patients

The physician is not expected to function as a psychiatrist or skilled psychotherapist. In his practice, however, he should always maintain a *medical attitude*. This means that the physician helps whenever possible and does nothing to make matters worse. Sometimes self-destructive patients are uncooperative, provocative and hostile. Such behavior makes the physician's task more difficult, but should be regarded as symptomatic rather than taken personally. The average physician will encounter half a dozen potentially suicidal patients a year and have 10 to 12 suicides in his practice during a long career. Suicide prevention is not his daily preoccupation but rather an occasional opportunity. The management of suicidal crises includes emergency medical and psychological support, plus consultation and referral in appropriate cases, and a special effort to keep in touch with patients while they are still suicidal.

*Emergency Medical Care.* Suicidal patients require extra time, not only for examination but for

management and follow-up care. Some suicidal depressions are precipitated by drugs, such as reserpine and occasionally antibiotics, or by withdrawal from sedatives or alcohol. Sometimes virus infections, nutritional deficiencies or hormonal disturbances are important factors. Often changes in previous medical treatment plans are indicated.

It takes extra time to reassure the anxious patient or explain to the suspicious. Some physicians wisely schedule emotionally disturbed patients at the end of consultation hours, so that extra time is available if needed. If a patient requires excessive time in the office or makes repeated emergency night time telephone calls, it may well be a signal to transfer the patient to a psychiatrist or to put him in a hospital.

*Use of Drugs.* Drugs are an essential part of the medical management of suicidal patients. For sleepless patients the rapid-acting barbiturates and other strong hypnotics are wonder drugs. They give an exhausted patient a chance to rest and recover. But these drugs are being misused. There were over a thousand deaths from barbiturates in California last year, most of them due to drugs prescribed by physicians. Prescriptions should not be dispensed or refilled casually. Repeated requests for hypnotics by a patient should warn the physician to review the case and possibly get consultation.

Tranquilizers, psychic stimulants and psychic energizers are used freely in our clinic. Recent articles<sup>6</sup> review present information on choice of drugs and dosage. This field is new and changing rapidly. During the last year we have been giving moderately anxious patients the tranquilizer chlor-diazepoxide, 30 to 100 mg a day. Agitated patients have received phenothiazines: Chlorprothixene, 75 to 200 mg a day, or thioridazine, 30 to 100 mg a day. Depressed patients were usually given amitriptyline, 30 to 150 mg, or imipramine, 30 to 200 mg daily.

I dispense tablets and psychotherapy simultaneously. I tell patients, "The drug industry spent a fortune developing these pills for you and millions of other patients like you." Side effects, such as dry mouth, are predicted, and the patient is instructed to call me daily or every other day to report. This facilitates our communication and provides for follow-up. Usually the patient gets better. If he feels worse on medication, I think seriously of getting him into a hospital.<sup>11</sup>

*Emergency Psychological Support.* Because of his position of trust and authority, the physician is ideally suited to give emergency psychological first aid. This includes: (a) Establishing communication with the patient; (b) reminding him of his identity; (c) involving family and friends; and (d) stimulating toward constructive action.

Suicidal patients are by the nature of their response to their difficulties, isolated and alienated from other people who could help them. They feel "different," changed for the worse, worthless. By taking the time to talk with him, the physician helps the patient to reestablish communication with the rest of the world. Psychological support is transmitted by a firm and hopeful attitude. Although the physician recognizes sympathetically that to the patient his problem is overwhelming and insoluble, at the same time he indicates that he has seen many other patients in similar crises who eventually recovered completely. Hope is a powerful medicine which should never be withheld.

The process of taking a medical history is in itself therapeutic. In reviewing his history, the patient is reminded of what he was in the past and who he is now—husband, worker, father and the like. Thus he recreates his sense of personal continuity and identity. In answering questions about his present problems, the patient widens his view of the world, alternative possibilities can be explored, and additional solutions are suggested. If the physician can help the patient break his overwhelming, giant-size problem down into several smaller, clearly stated and logically organized, man-size problems, it helps him overcome his panic and confusion.

*The Use of Family and Friends.* One of the key problems in suicide prevention is the appropriate use of families and friends. It is suggested that whenever possible the family physician talk to the relatives or friends of the patient who is in a suicidal crisis, especially if it is evaluated as an emergency. If the significant "others" have not appreciated the seriousness of the situation, they should be so advised. Often during an emergency there should be someone with the suicidal person at all times until the crisis is passed. An interview with the closest other person gives the physician a chance to decide whether that person can be supportive or whether he is, in fact, dangerous to the suicidal person because of carelessness, indifference or hostility. Some of the decisions



made about suicidal persons are family decisions; for example, the decision to put them in a hospital. Sometimes patients say, "My husband isn't interested" or "my wife doesn't care to bother," but a telephone call will usually reveal that relatives are concerned and cooperative. One interesting point is that where there is one suicidal patient in a family, there is often another person who is near suicide.<sup>5</sup>

*Constructive Action.* Suicidal patients are often overwhelmed by feelings of failure, paralysis and immobility, relieved in some by sudden impulsive spasms of action. Often the self-injury is a desperate attempt to regain the ability to initiate acts. Wherever possible, the physician should direct the patient toward planned and organized actions of a limited scope, which the patient can be expected to negotiate with a degree of success—for example, going to the physician's office for consultations and tests and making telephone reports to the physician at a certain time of the day. The patient might be asked to call a certain friend or take a simple psychological test. Persons who are recovering from suicidal states should be cautioned against prematurely resuming positions of great responsibility where initiative is required. More routine and limited tasks have a great therapeutic value, in that they take attention away from the patient's self preoccupation, and tend to create a feeling of confidence when they are successfully completed.

*Consultation and Referral.* Whenever possible, the physician should share some of the responsibility for the management of suicidal patients by discussing the situation with a colleague, associate or consultant. The most serious suicidal crises are best treated in a hospital, preferably psychiatric. The decision for psychiatric hospitalization of a suicidal patient is a full-fledged medical emergency, since about 15 per cent of suicides occur in persons who have had a recent recommendation of hospitalization but have not followed the recommendation. In hospitals, the same principles of suicide prevention apply. Physicians should pay attention to nurse's notes and patients' communications as possible clues to suicide.

In most patients, however, suicidal potentiality is less immediately critical, and out-patient treatment can be considered. If the patient has a long-standing, chronic personality disorder, or if his behavior has been obviously psychotic or has indicated severe emotional disturbance, or he con-

tinues to be suicidal for several weeks, a consultation with a specialist in the field of emotional problems is recommended. Most often this would be a psychiatrist, but clinical psychologists and psychiatric social workers are helpful in certain types of cases. Community agencies, such as social work and family service agencies, are very useful for assistance with reality problems such as finances, jobs, supportive care and home visits. Mental hygiene clinics or community-supported mental health centers are available in some places. In areas where there are no community or private agencies for care and where there may be no psychotherapists in private practice readily available, the physician will find the public health and mental health officer of the region able to offer considerable assistance and advice.<sup>3</sup>

After physicians, police officers deal most frequently with suicidal persons. Discussion and planning for suicidal emergencies between the police and the physicians of a community have proved beneficial for both professions and the public.<sup>5</sup> The legal aspects of detaining suicidal persons in hospitals for their own safety vary from state to state. In California several methods are provided, and physicians are encouraged to use their authority for this purpose.

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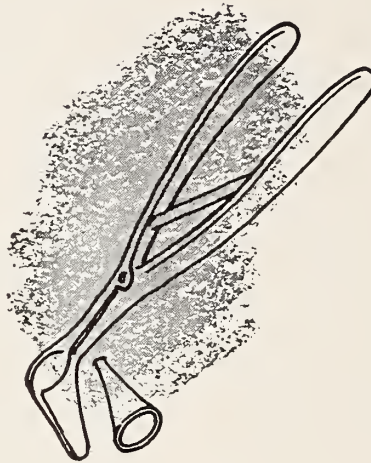
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# Hemorrhage During Long-Term Anticoagulant Drug Therapy

## Part III. The Relationship of Minor to Serious Bleeding

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■ *In a study of reports of 805 instances of spontaneous bleeding occurring among 2,189 patients receiving long-term anticoagulant drug therapy, 124 episodes were considered serious and 681 minor. There was no significant correlation of minor bleeding and serious bleeding.*

*Minor bleeding unassociated with excessive reduction of coagulability or an underlying organic lesion could not be considered, according to this evidence, an indication for discontinuance of anticoagulant drug therapy.*

*In apparently minor internal bleeding, however, hidden underlying organic lesions must be excluded. If gross hematuria occurs, renal lesions must be excluded.*

*Rectal bleeding must not be considered minor until gastrointestinal lesions have been excluded.*

MINOR HEMORRHAGE occurring during long-term anticoagulant drug therapy should be of minor importance *per se*—if the definition is correct. However, minor hemorrhage has acquired a rather sinister connotation to some physicians as a precursor of serious hemorrhage. Its correlation with serious hemorrhage—that which is potentially crippling or fatal—and with serious thrombosis should be clearly and quantitatively documented.

The serious hemorrhages can be broadly divided into two groups: (1) intracranial and gastrointestinal hemorrhages, which make up about 90 per cent of this group; and hemorrhages into various visceral sites, which largely account for the

remaining 10 per cent. Minor hemorrhages include purpura, hematomas, episcleral hemorrhage, epis-taxis and hematuria—all usually due to capillary breaks.

Ecchymosis and petechiae occurring in the first few days of coumarin drug therapy, especially in women with thrombophlebitis, may be a fore-runner of the rare and serious complication of gangrenous infarction and necrosis of the skin and subcutaneous tissues. This has not been reported during long-term therapy.

Discontinuance of the use of anticoagulant drugs is mandatory for serious hemorrhage but it is undesirable for minor bleeding, unless the episodes presage concomitant or subsequent serious hemorrhage. Regardless of the reason for stopping the drugs, an increased incidence of thromboembolism

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may occur within a short period.<sup>4,12,24</sup> The precise mechanism is controversial.

If, in addition to stopping the drugs, vitamin K1 is given, the risk of thromboembolism is heightened. Even with the bleeding extensive and the prothrombin activity excessively low, intravenous vitamin K1 may at times swing the coagulability to so high a level that fatal thrombosis ensues.<sup>7</sup>

The clinician might well ask, what is the importance of minor bleeding in heralding concomitant or subsequent serious bleeding? And, what is the importance of minor hemorrhage in initiating serious thrombosis if the drug is discontinued?

In the early days of anticoagulant drug treatment, the early detection of minor hemorrhage was an indication for stopping therapy. A positive microscopic or chemical finding of hematuria was regarded as a potential precursor of serious bleeding.

Fuller<sup>6</sup> regarded any sign of a bleeding tendency, however slight, as serious and its early recognition of great importance. He recommended the routine use of orthotolidine (occult test) for the detection of microscopic hematuria.

Even more recently, minor bleeding has been regarded as ominous. Lempert<sup>11</sup> warned of "slight bruising, even the slightest sign of hemorrhage, a little epistaxis or a little discoloration of the urine," saying that "presumably, this coincides with sudden profound changes in the thromboplastin factor or other factors."<sup>11</sup> At present, in most large clinics, anticoagulant drugs are not discontinued for more than a day or two at the most for minor hemorrhage, unless the prothrombin activity is excessively reduced. The definition of a "minor" non-threatening hemorrhage may depend, of course, on the apparent clinical severity. Often, neither the physician nor the patient considers diffuse purpura, petechia, ecchymosis, episcleral hemorrhage, hematomas or hematuria to be "minor."

Prandoni and Wright<sup>21</sup> when administering the drug for the first time in 1942, were naturally alarmed by subcutaneous hematomas and hematuria and "lost much sleep over this." Their experiences led to a fortunate delay in the release of the drugs until further studies could be carried out. The inclination to discontinue the drugs and administer vitamin K1 often may still be strong, but the risk of serious thromboembolism after

stopping anticoagulant drugs for minor hemorrhage may be as great as the risk after stopping the drugs for major bleeding. Sise<sup>24</sup> reported that "even after relatively minor bleeding such as hematuria and a small hematoma, fatal complications were observed."

Marshall<sup>12</sup> and Conrad and Rothermich<sup>4</sup> observed cerebral and coronary thrombosis as complications after stopping the drugs for bleeding.

How often minor hemorrhages portend concomitant or subsequent serious hemorrhage has not been adequately documented. Even those who strongly advocate the use of the orthotolidine test to detect microscopic hematuria have demonstrated no significant relation of the bleeding to serious hemorrhage.<sup>6,18</sup> Capillary fragility tests are of little value in predicting a tendency to serious bleeding from anticoagulant drugs.<sup>22</sup> The primary and secondary bleeding-time tests on capillaries of the skin described by Owren<sup>15</sup> have not been proved to correlate with the incidence of intracranial and gastrointestinal hemorrhages.

In a previous study of long-term anticoagulant therapy of 1,626 patients, 86 of 95 serious hemorrhages (90 per cent) were either intracranial or gastrointestinal.<sup>1</sup> The other nine were from various sites. No deaths occurred from renal hemorrhage, although hematuria is common.

## Material

I have analyzed all the spontaneous hemorrhages in a number of group studies involving 2,189 patients on long-term anticoagulant therapy in which data were given permitting answers to the following questions:

- How many serious hemorrhages were preceded by or were concomitant with minor hemorrhages?
- How many minor hemorrhages occurred without any associated serious hemorrhages?
- Was there any significant correlation between minor and serious hemorrhages?

The answers to these questions should furnish more precise evidence as to whether minor hemorrhages should be a guide as to subsequent serious bleeding.

## Results

The serious hemorrhages were considered those of intracranial or gastrointestinal origin or those from other sites known to be capable of killing



TABLE 1.—*Relation of Spontaneous Serious Bleeding to Minor Bleeding in Long-Term Anticoagulant Therapy*

<i>Authors</i>	<i>Number of Patients Treated</i>	<i>Number of Spontaneous Bleeding Episodes</i>	<i>Number of "Serious" Episodes</i>	<i>Associated Minor Bleeding Pre-existing or Concomitant</i>
Tulloch and Wright <sup>27</sup> .....	227	68	9	No correlation mentioned
Thomes, Scallen and Savage <sup>26</sup> .....	312	95	17	None
Pollard and coworkers <sup>20</sup> .....	139	61	10	None
Nichol and Borg <sup>14</sup> .....	78	41	6	None
Suzman, Ruskin and Goldberg <sup>25</sup> .....	82	12	2	None
Keyes, Drake and Smith <sup>10</sup> .....	121	54	5	None
Pickering <sup>19</sup> .....	195	48	5	None
Bjerkelund <sup>2</sup> .....	119	53	12	None
Fisher <sup>5</sup> .....	195	78	15	None
Groch et al. <sup>8</sup> .....	92	19	12	None
Borchgrevink <sup>3</sup> .....	103	10	3	None
Waler <sup>28</sup> .....	275	54	14	None
Peyman <sup>18</sup> .....	34	18	0	None
Fuller <sup>6</sup> .....	217	194	14	None
Total .....	2,189	805	124	None

or disabling. Among 2,189 patients on long-term anticoagulant treatment, there were 805 spontaneous bleeding episodes (Table 1). Of these, 681 were considered to be minor and 124 serious (5.6 per cent of the overall group). In none of the 124 serious episodes was there specific mention either of minor bleeding preceding the hemorrhage or of any concomitant minor bleeding. Although minor bleeding may have been present and not mentioned, it is probable that all bleeding sites were reported.

Bjerkelund,<sup>2</sup> on the contrary, in commenting on 53 instances of spontaneous bleeding, said specifically that there were no cases in which there was bleeding from several places at once.

None of the 681 minor hemorrhages progressed into serious bleeding. There was no significant correlation between minor and serious diffuse hemorrhage from toxic disease.

This in no way excludes the possibility of both minor and serious hemorrhage occurring simultaneously from prolonged toxic doses. Isolated cases attest this danger.

Poisonous doses of the coumarin drugs can induce the same kind of serious diffuse hemorrhagic disease in man that led to the discovery of the drug in the hemorrhagic sweet clover disease in cattle. Prandoni and Wright<sup>21</sup> in their early studies with Dicumarol® found that three patients had hematemesis in association with minor hemorrhages resulting from excessive dosage. Pastor, Resnick and Rodman<sup>17</sup> reported several instances of diffuse hemorrhage due to prolonged excessive doses of anticoagulant drugs. In these patients,

hematuria, ecchymosis and hematomas were associated with hematemesis following long periods of excessive dosage.

Most of the superficial capillary hemorrhages occurring with non-poisonous doses do not herald serious hemorrhage. Nontoxic doses seldom cause serious spontaneous hemorrhage except in the presence of a pre-existing bleeding lesion. Hematuria, the commonest minor hemorrhage, seldom requires more than reduction of the dose of coumarin drug or, at most, discontinuance for one or two days.

Owren<sup>16</sup> said he never gives vitamin K1 or a blood transfusion for hematuria, holding that because of the abrupt high coagulability induced, this treatment "is more dangerous than the bleeding." All minor bleeding arising internally, however, should be investigated to exclude internal lesions. Although nearly all the instances of hematuria are due to superficial capillary bleeding, the need for investigation for an underlying causative lesion is not lessened. Mild to moderate bleeding may arise from renal calculi. Gross hematuria, especially if it occurs with a desirable prothrombin level, may unmask a pathologic lesion. Hemley, Arida and Schwartz<sup>9</sup> reported two such instances, one in a patient with a polycystic kidney with multiple small papillary adenomas and the other in a patient with a hypernephroma. In answer to a questionnaire, Nathan and Kimball<sup>13</sup> received reports of 71 occult malignant renal tumors detected during anticoagulant drug therapy. In all patients with hematuria, a renal study is advisable. Thorough investigation is also indicated for rectal

bleeding. Apparent minor bleeding may unmask a carcinoma.<sup>13,23</sup> Although sigmoidoscopic examination is indicated for all patients having a complete physical examination, and especially for patients who are to be given long-term anticoagulant drug therapy, frequently it is not done.

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# Trophoblastic Disease

## Concepts of Management

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■ *Trophoblastic tumors are a notoriously unpredictable group in which metastasis may occur from histologically benign tumors and cause death, whereas a histologically malignant tumor may spontaneously disappear. Additional problems are created by the inability to accurately establish a diagnosis before abortion of molar tissue or development of metastasis.*

*In recent years chemotherapy has dramatically improved the prognosis of patients with choriocarcinoma. This fact, plus the importance of the time interval between onset of disease and the beginning of chemotherapy, makes close follow-up of patients with trophoblastic tumors imperative.*

*Concepts of therapy for trophoblastic tumors are rapidly changing. Indications for chemotherapy are broadening, especially in the areas of persistent and metastatic trophoblastic disease. As surgical intervention in the form of hysterectomy is becoming less important, the reproductive capacity of these young women is being preserved.*

*Astute diagnosis, appropriate therapy and active life-long follow-up are the essentials in the management of patients with trophoblastic disease.*

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HYDATIDIFORM MOLE is infrequently seen in an average practice. However, it remains an important diagnostic consideration because of the severity of its associated complications, its propensity for malignant transformation and, more recently, because of the efficacy of chemotherapy in the treatment of the benign and malignant forms.

The concepts presented here have been influenced by our experience in the management of trophoblastic disease at the Los Angeles County General Hospital, where a hydatidiform mole clinic was established five years ago, and by an

intensive review of over 150 patients with trophoblastic tumors treated during the past 15 years. An analysis of these patients is beyond the scope of this presentation but will be reported at a future date.

Before discussing management of the patient with hydatidiform mole, it is necessary to review and possibly renovate the classification of trophoblastic tumors.

### Classifications

Classification has always been a major problem in dealing with trophoblastic tumors. This difficulty has increased in recent years because chemotherapy is being used more and more liberally and surgical removal, which afforded an oppor-

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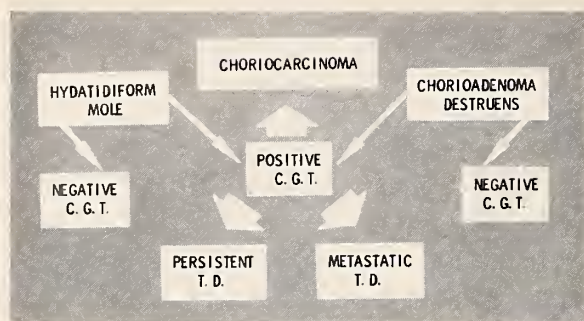


Chart 1.—Working classification of trophoblastic disease. Key to abbreviations: T.D.=trophoblastic disease; C.G.T.=chorionic gonadotrophin titers.

tunity for direct pathological examination, less and less. Difficulties have arisen in two areas. First, the inability to predict clinical behavior on the basis of the histologic features. Reports indicate that metastatic lesions may develop from benign hydatidiform mole and that death may result from these lesions although on microscopic examination they may have appeared benign.<sup>11,16</sup> On the other hand, histologically malignant choriocarcinoma has been known to undergo spontaneous remission without treatment. The second problem in classification occurs in patients who, having had a histologically benign mole, either have a metastatic lesion which is not readily accessible or have persistently elevated chorionic gonadotrophin titers when no other evidence of residual trophoblastic disease can be found.

In spite of these difficulties, some system of classification is necessary and that currently used in our clinic is shown in Chart 1. Patients originally classified as having hydatidiform mole and chorioadenoma destruens and whose chorionic gonadotrophin titers remain positive 60 days after initial treatment are reclassified as having either persistent or metastatic trophoblastic disease. These patients either have persistently elevated titers even though the existence of residual tumor cannot be demonstrated or have inaccessible metastasis when the original tumor was microscopically benign.

## Diagnosis

Unless obvious molar tissue is expelled from the uterus, there are no diagnostic tests to separate early pregnancy from hydatidiform mole. However, there are several clinical signs and laboratory tests which are of assistance in diagnosis. Among the clinical signs are hyperemesis gravidarum, development of preeclampsia earlier than the 28th

week of gestation, uterine bleeding and cramping and the presence of bilateral ovarian cysts, which may be very large. Any one or all of these signs may be associated with trophoblastic disease. It is frequently stated that the uterus is unusually large when hydatidiform mole is present. In our experience, one-third are smaller, one-third larger and the remaining third the correct size for the estimated period of gestation.

Radiographic studies may be of value if the gestation has progressed to the point where a fetal skeleton might be visualized. The presence of a fetal skeleton may be misleading, however, as mole and fetus can coexist. X-ray examination may also mislead where multiple gestation causes the uterus to enlarge excessively before the time of visibility of the fetal skeleton. An interesting technique, said to be diagnostic, is that described by Henrickse<sup>9</sup> in which a uterine angiogram is obtained.

Various serum determinations have been used as diagnostic aids including serum glutamic oxalacetic transaminase,<sup>17</sup> leucine aminopeptidase,<sup>13</sup> pregnanediol,<sup>7</sup> estriol<sup>4</sup> and chorionic gonadotrophin titer.<sup>6</sup> By far the most useful of these is the latter. Normally chorionic gonadotrophin is increasingly elevated to about the 60th day of gestation and then decreases to about the 100th day, after which relatively low levels persist until delivery. Titers are usually negative by four to six days later. Chorionic gonadotrophin levels are extremely sensitive indicators of trophoblastic activity and significant levels may be produced by minute groups of tumor cells. According to Delfs,<sup>6</sup> determination of chorionic gonadotrophin titers in serum are more significant than in urine, and spinal fluid titers are of no value. From the foregoing it is evident that high titers during the first 60 to 100 days of gestation are difficult to interpret, but after 100 to 150 days they may be significant. Of interest is the observation that unusually high titers may occur in subsequent pregnancies following treated and presumably cured choriocarcinoma.<sup>8</sup> The chorionic gonadotrophin titer assumes critical importance in follow-up.

The use of ultrasound as a diagnostic tool is also described.<sup>15</sup> Acosta-Sison<sup>1</sup> has described a test in which a blunt probe is gently passed into the uterus. If a normal pregnancy is present the probe will meet the resilient resistance of the membranes. If, on the other hand, a mole is present, the probe will pass deep into the uterine cavity



without resistance. In our limited experience this test has been unsatisfactory.

Taking all known tests into consideration, the unfortunate fact remains that unless molar tissue is passed, there is no diagnostic sign or test and rarely is a diagnosis of trophoblastic disease made before abortion. When considering the diagnosis and management of trophoblastic disease, we are confronted by three quandaries. First, the inability to consistently diagnose mole before the passage of tissue; second, the problem of the patient who has demonstrable but relatively inaccessible metastasis with only benign molar tissue having been removed from the uterus; and, third, what to do about the patient with persistently elevated chorionic gonadotrophin titers but no other evidence of trophoblastic disease.

### Surgical Therapy

Surgical evacuation of the uterus is the initial therapy in almost all patients with benign or malignant trophoblastic disease. This may be preceded by oxytocin stimulation, however, to induce cervical dilatation and partially empty the uterus. Curettage is by far the most frequently used method of uterine evacuation. While it is a relatively simple procedure, a number of complications may be encountered. The uterus containing a hydatidiform mole is usually large and very soft, and bleeding tends to be heavy until all molar tissue is removed. Before curettage is carried out, blood should be cross-matched for transfusion. An intravenous oxytocin infusion should be running and intravenous methergine given just before the procedure is begun. Another hazard is uterine perforation, and great care must be exercised to avoid it. Infection before or after operation is a common complication. While some investigators have advised a second curettage routinely 24 hours after the first, it has been our experience that not often is additional molar tissue removed if the first curettage was carefully done.

If the uterine fundus is above the level of the umbilicus it may be wise to empty it by hysterotomy rather than curettage, because in these large uteri the risk of perforation is great and total evacuation difficult. One should be careful to avoid spillage of trophoblastic tissue into the peritoneal cavity during operation. In patients over 35 years of age who have no desire for future children, hysterectomy is the treatment of choice. This selec-

tion of therapy is based on the increased incidence of malignant transformation in older women.

Subsequent curettage may be indicated at various times in the follow-up care of the patient with trophoblastic disease.

The value of hysterectomy and bilateral salpingo-oophorectomy in patients with choriocarcinoma is debatable. However, there is increasing evidence that it is not mandatory even when the tumor is apparently confined to the uterus. Some observers<sup>5</sup> have indicated that the cure rate with combined chemotherapy and hysterectomy is somewhat lower than that obtained with chemotherapy alone. However, an increase in remissions after chemotherapy in patients who have had oophorectomy has been reported.<sup>10</sup> Certainly the initial therapy for patients with choriocarcinoma or with metastatic or persistent trophoblastic disease should be medical rather than surgical.

### Medical Therapy

Chemotherapy of trophoblastic disease is one of the great medical accomplishments of the past decade. Before chemotherapy, choriocarcinoma was one of the most virulent of malignant neoplasms, affecting young women and quickly bringing death in the vast majority. At present most patients, even those with metastasis, can be cured.

Chemotherapy is useful in three major groups of patients: those with proven choriocarcinoma; those with metastatic disease but no tissue diagnosis of malignant change; and those with elevated chorionic gonadotrophin titers but no other evidence of disease. In addition, Acosta-Sison has advocated prophylactic use of chemotherapy in patients with benign hydatidiform mole.<sup>3</sup>

The most effective agent is methotrexate, a folic acid antagonist. Actinomycin-D, vincalcukoblastine sulfate and chlorambucil have also been successfully used either in combination with methotrexate or in the treatment of patients with tumors resistant to methotrexate.

Pre-treatment evaluation of the patient is imperative and should include a complete physical examination, blood cell count, urinalysis, x-ray film of the chest, serum chorionic gonadotrophin titer and liver function tests. If the specific gravity of the urine is less than 1.016 on a random sample, phenolsulphthalein and concentration tests should be done. Evidence of previous renal or hepatic disease may contraindicate chemotherapy or indicate need for reduced dosage.

Methotrexate is best given orally or intramuscularly in doses of 15 to 30 mg daily. The first course should be limited to five days so that individual sensitivity to the drug may be determined. Subsequent courses of therapy should be given at ten-day to two-week intervals or after all signs of toxicity have disappeared. Each course should be continued until the first sign of toxicity appears and then stopped, since toxicity may increase for four to seven days after discontinuing the drug. Although reactions may be noted in almost all organ systems, gastrointestinal and hematologic manifestations are the most reliable. Any oral ulceration or leukocyte count below 3,000 per cu mm should dictate termination of therapy especially in early courses.

It is important to realize the great variability in response to these agents. With this in mind the dosage might be increased beyond the usual limits of toxicity if the patient made a rapid recovery from early courses. In our experience the longest course was 12 days.

The most sensitive indicator of trophoblastic activity, and therefore the best indicator of effectiveness of therapy, is the serum chorionic gonadotrophin titer. This titer should be determined at the beginning and at the end of each course of therapy. An additional one to three courses should be given after chorionic gonadotrophin titers have become negative.

Change in therapeutic agent should be based upon one of three criteria: first, lack of response after four courses of methotrexate; second, chorionic gonadotrophin titers continuing to rise in spite of therapy; and, third, toxic response to methotrexate too great to continue therapy.

### Follow-up

The critically important factor in management of benign trophoblastic disease is adequate follow-up, for only by this means will early detection of persistent or metastatic trophoblastic disease or choriocarcinoma be possible. This is especially important since the efficacy of chemotherapeutic agents in patients with choriocarcinoma is directly related to the length of time the disease has been present before the beginning of therapy.<sup>10</sup>

Certain factors are associated with an increased incidence of malignant change and therefore increase the need for close observation. Among these are advanced age, pronounced trophoblastic proliferation, uterine enlargement greater than the

size consistent with five months of gestation, absence of palpable ovarian cysts, pulmonary tuberculosis and fresh mating.<sup>2,14</sup>

After uterine evacuation has been accomplished and baseline studies obtained (film of the chest, blood cell count, pelvic examination and serum gonadotrophin titer), the patient may be discharged and observed as an outpatient at weekly intervals. At each visit a careful pelvic examination must be done and baseline studies repeated. Since a serum gonadotrophin titer of around 5,000 is necessary for a consistently positive pregnancy test, biologic tests may be inadequate and should not be relied on for these early follow-up visits. Weekly x-ray films of the chest are important inasmuch as we have seen widespread pulmonary metastasis develop during this period of time in a previously radiographically negative chest.

While chorionic gonadotrophin titers become negative in four days after normal pregnancy, it should be borne in mind that in molar gestation nearly 40 per cent of patients have positive titers even after two months. Therefore, a second curettage is necessary only if titers are positive more than two months after abortion or if they are rising or over 20,000 units at the end of one month.

During follow-up visits special consideration should be given to symptoms of gastrointestinal bleeding, hemoptysis or vague neurologic complaints, any of which may indicate early metastatic disease.

After the gonadotrophin titer has been negative twice in succession, the patient may be seen at monthly intervals for one year and then yearly. Any suggestion of trophoblastic activity at any time indicates need for further diagnostic study.

The follow-up regimen in cases of choriocarcinoma or persistent or metastatic trophoblastic disease differs only in that the patient should be examined weekly for one to two months, and then monthly for two years. Since gonadotrophin titers will be negative after termination of chemotherapy, any subsequent elevation should be considered an indication of reactivation of disease and reason for prompt resumption of therapy.

Contraception is a vital part of management and it should be stressed. It is important because of the difficulty which is encountered in differentiating early pregnancy from recurrent trophoblastic disease. Contraception should be practiced for one



year by patients who have had benign moles and at least two years after treatment for choriocarcinoma.

What is the correct advice for the patient who ignores contraception and is seen within a year with amenorrhea, enlargement of the uterus and elevated gonadotrophin titers? Individual circumstances would certainly affect judgment, but in general a diagnostic dilation and curettage is indicated. This decision is based on the opinion that sacrifice of an early pregnancy is preferable to delay in treatment of a possible choriocarcinoma.

After the patient has been without evidence of disease for one or two years, there is no contra-indication to pregnancy. There is no evidence of infertility or increase in congenital malformations in pregnancies occurring in women who were previously treated with methotrexate. As many as eight moles have been reported in a single patient.<sup>11</sup> However, there seems to be no increase in the over-all incidence of molar degeneration in subsequent pregnancies.

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# Comparative Evaluation of Rheumatic Activity

## *A Study of Relationship Between Histologic Changes and Serologic Test Results in Cardiac Surgical Patients*

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■ *Atrial or ventricular myocardium from patients with surgically corrected rheumatic valvular disease was studied for rheumatic lesions in 86 cases. Histologically active Aschoff bodies were found in 20 per cent of the cases. A slight, but statistically not significant relationship was demonstrated in comparison of elevated serologic tests for rheumatic activity with the presence of Aschoff bodies.*

DEVELOPMENT of surgical procedures to correct valvular deformities of rheumatic heart disease has provided the opportunity to study the relationship between histologic changes in atrial and ventricular myocardium and classic serologic tests for rheumatic activity, and to relate these findings to operative mortality.

The Aschoff body, most frequently observed in the atrial appendage,<sup>5</sup> has been considered to be the characteristic lesion of the active phase of the rheumatic process.† Thomas and coworkers<sup>23</sup> and Decker and coworkers compared lesions in the atria with those in the heart as a whole and concluded that the presence of Aschoff bodies in atrial appendages parallels the presence of Aschoff bodies in the remainder of the heart.

Several investigators<sup>5,14,20</sup> have reported no correlation between the presence of Aschoff bodies and elevated antistreptolysin-O titers (ASO), C-reactive protein (CRP), and erythrocyte sedimentation rates, and also no correlation between Aschoff bodies and operative mortality.<sup>14,20</sup> In contrast, Biorck and coworkers<sup>2</sup> indicated that there was some evidence of correlation between active rheumatic carditis, as manifested by Aschoff bodies, and elevated ASO titers; and Brusca and coworkers<sup>3</sup> demonstrated a strongly positive correlation between Aschoff bodies, CRP and ASO titers.

In view of this variance, and because cardiopulmonary bypass techniques permit surgical treatment of patients with more advanced forms of rheumatic heart disease, it was felt that a review of a group of patients who underwent surgical correction for valvular deformities of rheumatic etiology, with correlation of the presence of Aschoff bodies, elevated ASO titers, positive CRP and mortality, might help elucidate this problem.

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†Reference Nos. 9, 15, 18, 24, 26.



## Cases Reviewed

The cases included in this survey were those of patients with rheumatic valvular disease operated on by one surgical team at the Hospital of the Good Samaritan Medical Center in Los Angeles in the period January 1961 to August 1965. The atrial appendage or other portions of the myocardium were available for pathologic evaluation.

The group included 86 patients, 61 females and 25 males, ranging in age from 9 to 74 years. This sex distribution is similar to the reported overall incidence of rheumatic heart disease, but the preponderance of females is not as great as was reported in 1955 in a similar group of patients operated on in this same institution.<sup>23</sup>

Multiple sections of either right or left atrial appendage, or a portion of ventricular myocardium were examined for the presence of Aschoff bodies.

Of the 86 patients, 63 had ASO determinations (method of Todd), and 59 had CRP determinations (method of Todd).

For the group as a whole, there were nine deaths in the operative or postoperative period.

## Results

The findings of our review are tabulated in Table 1. Aschoff bodies were found in 17 of 86 cases (20 per cent), with 14 occurring in females and three in males. The ASO titers (greater than 50 Todd units), as well as CRP, were abnormal in a greater proportion of cases in which Aschoff bodies were demonstrated, but the difference is not considered to be statistically significant. Similarly, Aschoff bodies were found more often in

patients with elevated ASO titers and in patients who were CRP positive.

Postoperative mortality was 5.8 per cent in the group with Aschoff bodies (one death in a group of 17), 12 per cent in the group with elevated ASO titers and 15 per cent in the group with positive CRP.

In 49 of the 86 cases reviewed, operation was done with cardiopulmonary bypass methods. Eight of the nine deaths occurred in this group.

## Discussion

Our findings indicate a slight but apparently not significant correlation between the presence of Aschoff bodies in the atrial or ventricular myocardium and response to serologic tests, which agrees with the studies by Tedeschi<sup>20</sup> and others<sup>5,14</sup> and raises the question of whether Aschoff bodies are pathognomonic for active rheumatic heart disease. This was Aschoff's impression, when in 1904 he noted the presence of small structures in the atrial and ventricular myocardium at necropsy in 11 cases of clinically active myocarditis associated with rheumatic heart disease.<sup>1</sup> These nodules were carefully described by him, and his criteria are still used today. In the cases reviewed here, the Aschoff bodies found and accepted were oval or football-shaped structures lying in the loose connective tissue of the subendocardium or near a blood vessel in the myocardial interstitium. Large cells with usually a basophilic cytoplasm and single or multiple vesicular nuclei were present in the periphery. Central foci of fibrinoid necrosis and degeneration were required for identification. Small, round, fibrotic structures, possibly developed from old Aschoff bodies, were seen in the subendocardium in some cases, but in this study they were not considered to be histologically active Aschoff bodies.

It is interesting to note that the reported incidence of Aschoff bodies has been decreasing. In the period from 1925 to 1935, in three autopsy series,<sup>8,17,21</sup> the reported incidence ranged from 87.5 per cent to 90 per cent. In the period from 1950 to 1955 numerous investigators reported incidences ranging from 35.9 per cent to 55 per cent.\* Still others have reported incidences below 25 per cent.<sup>7,20</sup> Tedeschi,<sup>20</sup> Tragerman<sup>23</sup> and Saphir<sup>18</sup> all noted this discrepancy and related it to differences in the sampling and the histologic criteria of different observers.

\*Reference Nos. 2, 4, 6, 12, 13, 16, 19, 23.

TABLE 1.—*Correlation of Incidence of Aschoff Bodies and Abnormal Serologic Tests*

	Elevated ASO Per Cent	Positive CRP Per Cent
Patients with Aschoff bodies		
17 (20 per cent).....	79	36
Patients without Aschoff bodies		
69 (80 per cent).....	54	20
	Aschoff Bodies Present Per Cent	Positive CRP Per Cent
Patients with elevated ASO		
37 (59 per cent).....	31	26
Patients with normal ASO titer		
26 (41 per cent).....	12	23
	Aschoff Bodies Present Per Cent	Elevated ASO Titer Per Cent
Patients with positive CRP		
13 (22 per cent).....	38	69
Patients with negative CRP		
46 (78 per cent).....	20	56

Our strict criteria for acceptance of Aschoff bodies may in part explain our finding of only a 20 per cent incidence, even though in our series as well as in others, patients with obviously active rheumatic heart disease were excluded from surgical procedures.

Laboratory methods still used to exclude patients from surgical treatment include the ones evaluated in this study. Even with strict histologic criteria, there is only a slight correlation of positive serologic tests with the presence of histologically active Aschoff bodies. This raises the question of whether these procedures are useful for this purpose. Other tests, such as the recently described methoxytryptamine excretion test<sup>10</sup> may become refined and contribute more to patient evaluation.

The finding that only one of the 17 patients with histologically active Aschoff nodules died postoperatively, as compared with nine deaths in the entire group of 86 patients, indicates that, at least when the patients with obviously active and clinically evident rheumatic heart disease are excluded, the presence of Aschoff bodies or abnormal serologic tests does not indicate a poorer than average surgical prognosis.

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# Smoking and Pregnancy

## A Statistical Study of 5,659 Patients

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■ *The outcome of 5,659 pregnancies was recorded over a period of six years. The group was divided into 2,630 smokers and 3,029 non-smokers.*

*Smoking was associated with increased incidence of premature babies, but not increased infant mortality.*

*This study confirms the findings of other investigators.*

THE PRESENT CONCERN about the effects of tobacco-smoking upon health seems to warrant publishing our own observations on the effect of smoking on pregnancy.

During a six-year period between 1952 and 1958, 5,659 obstetrical patients at the Palo Alto Medical Clinic were classified as smokers or non-

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smokers. The final outcome of each pregnancy was noted and the results are shown in Table 1.

These results show that maternal smoking is associated with premature delivery at a statistically significant level, but does not affect the infant mortality. Smoking did not increase the incidence of spontaneous abortion in this study. However, it is noted that many abortions occurred before the women registered for prenatal care. Unfortunately these could not be included.

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TABLE 1.—*Outcome in 5,659 Pregnancies*

<i>Total</i>	<i>Smokers 2,630</i>	<i>Non-Smokers 3,029</i>	<i>Total 5,659</i>	<i>Chi Square</i>	<i>Signifi- cance</i>
Abortion.....	107	126	233	0.029	no
Premature.....	88	66	154	7.68	yes
Survived.....	71	55	126		
Stillborn.....	12	5	17		
Neonatal death.....	5	6	11		
Full Term					
Stillborn        } .....	12	21	33	1.327	no
Neonatal death } .....					
Total fetal mortality.....	136	158	294	0.0049	no

# Cryptococcus Neoformans in Pigeon Feces In San Francisco

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San Francisco

■ *Typical Cryptococcus neoformans was isolated from one of 10 specimens of pigeon feces collected in downtown San Francisco. This isolation from a small sample suggests considerable prevalence of this important pathogen and tends to confirm that it is ubiquitous.*

SO FEW are the cases of cryptococcosis diagnosed in San Francisco hospitals that one might conclude the disease is a rare one. However, the recovery of *Cryptococcus neoformans* from pigeon feces in San Francisco and a review of recent publications suggests that cryptococcosis may not be uncommon.

The association of *C. neoformans* with pigeon feces was first reported by Emmons in 1951.<sup>2</sup> Since that time, additional studies have demonstrated the ubiquity of *C. neoformans* in pigeon feces.<sup>3</sup> Perhaps the most dramatic demonstrations were the recovery of this organism from pigeon lairs in the dome of the Nation's Capitol in the District of Columbia and from soil in a park on Pennsylvania Avenue there. *C. neoformans* was isolated from 41 of 107 pigeon nests in Cincinnati by Kao and Schwarz<sup>7</sup> and from 72 of 201 collecting sites within New York City by Littman and Schneierson.<sup>8</sup> The latter found that pigeon feces collected from indoor sites (pet shops, markets and private homes) were more heavily and more frequently infected than those collected from unprotected outdoor sites.

*Cryptococcus neoformans* has also been recovered from the excreta of other birds<sup>13</sup> and

from soil contaminated with bird droppings.<sup>1</sup> It has been recovered from fruit juice, milk and the slime flux of mesquite<sup>4</sup> and has been responsible for epizootic bovine mastitis.<sup>12</sup> Infections in both domestic and wild animals have been reported.

A review of cases of pneumonitis in persons who had cleaned church belfries and other buildings covered with pigeon feces led Emmons to believe that an acute form of pulmonary cryptococcosis is probably not infrequent in persons who have exposure to air heavily laden with dust containing dried pigeon feces, although he was unable to prove that these patients had cryptococcosis.<sup>3</sup>

Procknow and associates in Chicago, however, recently reported a case of disseminated cryptococcosis in which, they believe, the initial pulmonary infection came directly from the inhalation of dust infected by pigeon feces.<sup>10</sup> They expressed belief that a companion of the patient, who had recovered from "pneumonia" that had not been etiologically diagnosed, had had pulmonary cryptococcosis. They were able to isolate *C. neoformans* with ease from specimens of pigeon feces taken in a dusty abandoned building in which both the patient and his companion had trapped pigeons before the symptoms of pulmonary disease developed.

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## Present Study

To determine the presence of *C. neoformans* in San Francisco, one specimen of pigeon feces was collected from the exterior of each of ten large public buildings. Following emulsification of a teaspoonful of each specimen in 10 ml of saline solution containing 50 mg of chloramphenicol and 40 mg of streptomycin per milliliter, two procedures for isolation were used. One-half milliliter of each of the ten suspensions of feces was injected intraperitoneally into each of four male white mice. At autopsy, approximately one month following inoculation, the brain, liver and spleen of each mouse were cultured on Sabouraud agar containing 50 mg of chloramphenicol per ml. No yeasts resembling *C. neoformans* were recovered from these mice.

In addition to the direct inoculation of mice with each fecal specimen, 0.5 ml of each suspension was inoculated on plates of Sabouraud agar containing 50 mg of chloramphenicol per milliliter and the plates were incubated at 37°C. Mucoid colonies of encapsulated yeasts appeared on plates from four specimens. These encapsulated yeast-like organisms were each suspended in saline solution and inoculated intraperitoneally or intracerebrally into groups of three mice. After approximately one month these mice were killed and pieces of brain, spleen and liver were inoculated on Sabouraud agar containing chloramphenicol. An encapsulated yeast was recovered from the brain, liver and spleen of two of three mice inoculated intracerebrally with one of the cultures. It was also recovered from the brain and spleen of one of three mice inoculated intraperitoneally with the same culture. Another mouse of this group died but autopsy was not done. No encapsulated yeasts were recovered from the tissues of the mice inoculated with the other cultures.

The recovered encapsulated yeast was identified as *Cryptococcus neoformans* by its mouse pathogenicity as well as by its ability to hydrolyze urea, by its growth at 37°C and its failure to produce hyphae on corn meal agar. This organism was not abundant in the fecal specimen from which it was isolated. Only five colonies had appeared on the original plates inoculated with 0.5 ml of the saline solution suspension of the feces. No yeasts were recovered from the mice which had received this fecal specimen directly.

The recovery of *C. neoformans* from one of 10 pigeon fecal specimens cannot indicate the true

incidence of this organism in San Francisco. It is an indication, however, that the climate famous and unique to San Francisco is no deterrent to the development of *C. neoformans* in pigeon feces which accumulate in large quantities throughout the city and that *C. neoformans* might be found to be as common in San Francisco as in New York City or Washington, D.C. if searched for more thoroughly.

Hasenclever and Emmons showed that many strains of *C. neoformans* occurring in nature are as virulent for the white mouse as those isolated from human infections.<sup>5</sup> This introduces the question of why clinical cryptococcosis is rare when so many persons probably have daily contact with virulent strains. Resistance to the development of clinical cryptococcosis is adequate in the normal person but there is a fairly high incidence of cryptococcosis as a secondary finding in lymphoma-leukemia patients.<sup>6</sup> Apparently the anti-infection mechanism is grossly impaired by lymphoma or leukemia. This high incidence rate also indicated such patients may encounter a serious hazard when they frequent areas where dried pigeon feces accumulate.

Until recently there has been no reliable skin test antigen for detecting present or past infection with *C. neoformans*. Salvin and Smith have now developed an antigen which appears to be useful.<sup>11</sup> Following the discovery of three cases of cryptococcosis in an Oklahoma town this antigen was used in a small survey.<sup>9</sup> Twenty-six of 83 persons had a delayed skin test reaction to cryptococcin and were nonreactive to histoplasmin and coccidioidin. This finding suggests that cryptococcosis may not be rare and that this disease may have some similarities to the benign pulmonary forms of histoplasmosis and coccidioidomycosis. Further study is needed.

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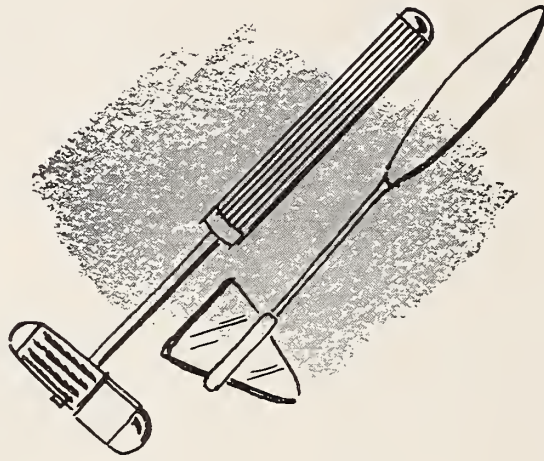
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# ULCERATIVE COLITIS

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DURING THE PAST DECADE such advances have been made in the treatment of ulcerative colitis that, although it remains an unpleasant disease, the mortality rate is not as high as it was 20 years ago. Developments in understanding of the pathogenesis of the disease have not kept pace with therapeutic advances; nevertheless, reliable data are now being collected which may serve to reveal the extent of our ignorance and stimulate rewarding inquiry.

There are many diseases involving inflammation and ulceration of the colon in which causal factors are well established. However, in civilized communities and in temperate climates, the great majority of patients with regional or total inflammatory disease of the colon will be classified as having chronic non-specific colitis, for which no cause is apparent. Clinical, histological and epidemiological studies suggest that ulcerative colitis is a disease in its own right; it is still uncertain whether the pathogenesis is due to single or multiple factors.

## Etiology and Pathogenesis

As with other chronic inflammatory disease of the gastrointestinal tract in which the cause is unknown, infective, immunological, nutritional and psychological factors have each had their share of proponents. There is no good evidence that the disease occurs spontaneously in animals and thus far there seems to be no convincing model of the disease in the experimental animal. Many attempts have been made to find an infective cause for ulcerative colitis but, although at various times *Shigella* infection, a diplococcus, a bacterium, *Staphylococcus aureus*, entero-viruses and various fungi have all been implicated, such claims have not

withstood criticism, and the possibility that some if not all cases of ulcerative colitis may be due to a specific microorganism is unproven. However, Felsen produced data showing a much higher incidence of ulcerative colitis and of regional enteritis in patients involved in an outbreak of bacteriologically proved bacillary dysentery. Further, internists familiar with ulcerative colitis will have noted previously healthy persons who have attacks of acute enterocolitis at the same time as other members of their group or family, then do not have remission when the others do but go on to have chronic ulcerative colitis. Taylor and True-love<sup>19</sup> noted that there are at least four possibilities which can be advanced to explain how a short-lived infection may induce chronic disease. First, by damaging the intestinal mucosa, the infection may set off autoimmune processes which are self-perpetuating. Second, non-pathogenic bacteria normally living as harmless commensals in the lumen of the bowel may be enabled to invade the intestinal wall and thus sensitize the host to one or more of the antigens of his own intestinal flora; or these bacteria may react with the components of the damaged mucosa to form complex antigens. Third, there may be immunological cross-reactions between components of certain strains of microorganisms and colonic or other gastrointestinal tissues, as between human heart tissue and group A streptococci, as postulated by Kaplan and his group in rheumatic fever. Fourth, the damaged mucosa may allow the entry of antigenic dietary protein which then induces a hypersensitivity state which becomes chronic.

The chronic inflammatory changes seen in ulcerative colitis have suggested to many that immunological reactions are involved either in the pathogenesis or in the perpetuation of the disease. Hypersensitivity reactions to three different types of antigen might play a primary part: The antigen

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might be alimentary, such as a food protein or some drug; it might be bacterial; or it might be a component of the patient's own tissues. Andresen, and later Rowe, particularly, have emphasized the role of dietary antigens in ulcerative colitis, but, apart from a recently published study of the effects of excluding milk protein from the diet in ulcerative colitis, there have been no convincing published studies to support this concept.<sup>21</sup>

Skin testing has not proved valuable in establishing sensitivity to any particular food, and attempts to demonstrate local tissue hypersensitivity by injecting various food extracts directly into rectal mucosa have not yet been evaluated in a scientific manner. Studies of circulating antibodies to dietary proteins have been made but, although a higher incidence of high titer serological reactions has been reported in a number of studies, there seems to be no correlation between high-titer reactions and response to exclusion of the appropriate protein from the diet. At least one study has suggested that early artificial feeding with cow's milk may predispose to ulcerative colitis in later life, but the reason for such an association remains obscure.

MUCH HAS BEEN published in the last five years suggesting that autoimmune reactions may occur in ulcerative colitis. The first study was published in 1959 when the Swedish workers, Broberger and Perlmann, reported the presence of auto-antibodies to human colon in a large proportion of specimens of blood obtained from children with ulcerative colitis. The antigen they used was extracted from human fetal colon (which was used because it was germ-free), and positive tests were obtained using hemagglutination and gel-diffusion. There was no antibody reaction in blood from healthy control children. However, some positive reactions were obtained when extracts of fetal liver and kidneys were used; and, further, positive reactions with colonic extracts were sometimes obtained when blood from patients who had rheumatoid arthritis, systemic lupus erythematosus, chronic hepatitis and the nephrotic syndrome was used. In other studies using the blood of adults with ulcerative colitis, the incidence of positive results was far lower, and the reason for this remains unknown. Whether the circulating auto-antibodies exert a harmful action on the colon is uncertain. Positive-reacting blood has not been shown to affect fetal colonic epithelial cells growing in tissue

culture. Indeed, by analogy with certain autoimmune experimental diseases in animals, there are theoretical reasons for expecting that circulating auto-antibodies may exert a protective effect on the appropriate tissue. By contrast, when the peripheral white blood cells from patients with ulcerative colitis are set up with fetal colonic epithelial cells, some indications of cellular damage may be obtained, a phenomenon that does not occur when white blood cells from healthy subjects are used.

The colonic antigen used by the Swedish workers and by other groups appears to be a lipopolysaccharide, and recent work has shown that it may share antigenic determinants with lipopolysaccharide extracts of coliform organisms. The possibility arises that the chain of events in the development of autoallergy to colonic tissue in ulcerative colitis is first the development of hypersensitivity to some component of the intestinal flora, the establishment of a delayed hypersensitivity reaction and finally a destructive action of sensitized cells on the endogenous target, namely some component of colonic mucosa. It must be stressed that this is highly speculative and there is at the moment no experimental model even to support the idea. An excellent review of this field by Broberger is available.<sup>2</sup>

Nutritional factors have been held by some investigators to be responsible for the change in ulcerative colitis but there is no evidence that any nutritional deficiency occurs before the onset of the disease. Lumb and Protheroe expressed belief that degeneration of epithelial cells at the bases of the crypts of Lieberkühn is the earliest lesion in ulcerative colitis, and they speculated that this may be due to an induced defect in cell-turnover. The fact that the use of folic acid antagonists may occasionally produce colitis in human subjects and that such agents are known to produce mitotic arrest in epithelial cells, does raise the possibility that there is some as yet undefined nutritional deficiency present, but good evidence is lacking.

Finally, because there have been so many proponents of the theory, it is impossible to overlook the view that this disease is essentially a psychosomatic disorder. The term is assumed to imply that a primary psychological disturbance may create pathological changes in the colon. Sterne's Tristram Shandy makes a very effective and pertinent comment:

"A man's body and his mind, with the utmost reverence to both I speak it, are exactly like a



jerkin, and a jerkin's lining; rumple the one, you rumple the other. There is one certain exception however in this case, and that is, when you are so fortunate a fellow, as to have had your jerkin made of gum-taffeta, and the body-lining to it of a saracenet, or thin persian."<sup>18</sup>

This sums up succinctly some of the points made recently by Powles,<sup>15</sup> which could apply equally well to any disease in which psychological factors are believed to be playing a special causative role. To establish a relationship it is necessary to demonstrate that factors recognized as stimuli of psychological disturbance precede the onset of the disease or a relapse more frequently than they would by chance, or that the host possesses a special psychological diathesis, or that the emotional trauma has significant quantitative or qualitative properties. The difficulties are considerable and the problem is unresolved. Murray, when a medical student in 1930, was the first to report the impression that there might be an association between emotional stress and onset of symptoms of ulcerative colitis. Many supporting reports from Engel and others have appeared since. Further, the experience of all internists who actively engage in treating ulcerative colitis is that stressful episodes may sometimes precede relapses. But this is only impression. Psychotyping of patients with ulcerative colitis or their close relatives has never been done on a prospective basis but only after development of the disease. Powles himself emphasizes the difference between an ulcerative colitis patient in relapse and in remission. The emotional response to a highly unpleasant disease needs no emphasis. Demonstration of the value of psychotherapy in controlled trials is a contribution to therapy but not necessarily to our understanding of the cause of the disease. Nevertheless there are many possible ways in which psyche and colon could interreact—the influence of emotional state on intestinal motility and on hypersensitivity reactions, to name only two—and this is an interesting area which must inevitably develop in future.

The increase in interest in ulcerative colitis in recent years is one facet of the enormous increase in research into gastrointestinal disease as a whole. It is a reasonable expectation that our knowledge of the disease will now increase at high speed.

## Pathology

Until very recently studies of tissue changes in ulcerative colitis were confined to the rectum and

colon and occasionally to the terminal ileum. Diffuse inflammation of the mucosa of affected bowel occurs in all cases. In the early stages hyperemia and mucosal granularity may be the only changes noted, but as the disease progresses, which it may do at an extremely variable rate, multiple, ragged ulcerations of the areas of inflammation occur, resulting in exudation of lymph, polymorphonuclear cells and erythrocytes to a variable degree. The inflammatory process usually starts in the upper rectum and pelvic colon. It may spread back to involve the entire colon, either rapidly or over the course of years. Pancolitis may be present when the disease is first diagnosed. The disease process characteristically stops short at the ileocecal valve, but occasionally it may be seen on radiological examination and at surgical operation to have spread into the terminal few centimeters of the ileum, this being termed backwash ileitis. Microscopically, the distribution of inflammation tends in both chronic and acute cases to be limited to the lamina propria, but if the disease is severe and of long standing the inflammation may penetrate through the muscularis mucosae into the submucosa. Deep ulcers may be formed in this way, and these may involve the muscle coats of the colon and occasionally lead even to perforation. In the acute disease the mucosa shows hyperemia and a heavy infiltration with various types of inflammatory cell of which the polymorph may be the most frequent, although an eosinophilic infiltration is quite common. The crypts of Lieberkühn may show inflammatory infiltration with loss of epithelial surface, thus forming so-called crypt abscesses. In the chronic disease the mucosa may show considerable flattening and loss of normal structure. The inflammatory cells are predominantly mononuclear, both plasma cells and lymphocytes. During healing, considerable granulation may occur at sites of frank ulceration, which become covered with epithelium to form so-called pseudo-polyps.

Electron microscopy of the colonic mucosa in ulcerative colitis has demonstrated some separation of epithelial cells by granular material of uncertain nature and it has been noted too that the tips of the microvilli of these epithelial cells are abnormal; small excrescences, which have been named "clavate fimbriae," may be seen to be attached by stalks to the microvilli. The distribution of enzyme activities determined by histochemical methods can be seen to be different in ulcerative

colitis mucosa from the normal; the highest concentrations of certain enzymes in ulcerative colitis tend to be found on the luminal borders of epithelial cells rather than in the basal parts of the cell, as in normal mucosa. However, normal mucosa from patients with ulcerative colitis shows a normal enzyme distribution. It has also been suggested that microsomal dislocation in the epithelial cells occurs in ulcerative colitis. Whether these changes are peculiar to ulcerative colitis is not known; neither is their significance.

Recently there has been some suggestion that the mucosa of both stomach and small bowel undergoes changes in ulcerative colitis.<sup>16</sup> Gastritis is said to occur frequently, although there have so far been no proper studies to determine whether its incidence is significantly higher than in an apparently healthy population or in groups of patients with other chronic, debilitating diseases. There is some suggestion that, as colitis remits, gastritis may do likewise. The jejunal mucosal pattern during attacks of ulcerative colitis may be abnormal, with blunting and fusing of villi and low grade inflammatory infiltration; it remains to be shown if these changes are associated with a significant degree of disturbance of absorption.

### Incidence of the Disease

The incidence of ulcerative colitis increased greatly in at least two civilized countries in the temperate zone in a recent ten-year period, for no obvious reason.<sup>7,9</sup> Geographical differences are becoming evident. Thus, in Britain, where the incidence of ulcerative colitis seems to be higher than in the United States, one case of regional enteritis occurs for every eight of ulcerative colitis. In Baltimore the ratio is nearer 1:2, and our own experience in California conforms to the Baltimore data.

Studies in the United States have attested a greater incidence of both ulcerative colitis and regional enteritis in Jews; and the recently reported finding of a significantly low incidence of ulcerative colitis in homozygous Rhesus *cc* persons explains this phenomenon, since *cc* has a low frequency in Jews. There is no evidence that the disease is more severe in Jews.

Despite the many reports of several members of the same family being affected with the disease, a significant familial factor remains to be proved. Further, there are no published data which clinch a definite genetic predisposition to ulcerative co-

litis; as with most human diseases, separation of genetic and environmental influences is extremely difficult.

### Clinical Features of Ulcerative Colitis

Recent reports of large series of patients with ulcerative colitis have permitted more precise statements about the mode of onset, the incidence and the prevalence of the disease.<sup>4</sup> It is relatively uncommon in childhood, but in three quarters of all cases the onset occurs between the ages of 15 and 49, with the peak in the fourth decade. In England, with increasing age women show an increasingly greater liability to the disease than men; in Sweden the reverse is the case. When the disease starts in childhood males may predominate. A study from Oxford has shown that in the past decade there has been a decided improvement in short-term fatality rates in patients referred for hospital treatment. This is partly due to a larger proportion having only mild disease, reflecting earlier diagnosis and also a recognition by family physicians of the value of early intensive treatment in hospital. Part of the improvement lies in a pronounced decline in mortality in patients with disease of moderate severity, which is due presumably to improvement in treatment.

### Diagnosis

The onset of ulcerative colitis may be acute or gradual. The first symptom may be the passing of small amounts of blood from the rectum, usually after defecation; it may be the onset of diarrhea or the passing of excessive amounts of mucus. A recent study showed that hemorrhage is the commonest presenting symptom in the young, diarrhea in the old. Children, especially, through reticence about discussing the bowels, may not complain of the symptoms of the disease. Dull, suprapubic pain is common but is rarely severe, in contrast to the often sharp pains of regional enteritis. There may be no systemic disturbance; but with severe and extensive disease, fever, weakness, malaise and weight loss occur. Sometimes one of the complications of ulcerative colitis—either local such as anal fissure, or systemic such as arthralgia or pyoderma gangrenosum or unexplained fever—may be the presenting symptom. In children failure to grow may be the presenting feature.

A negative result of examination of stools for pathogens will exclude many specific causes of



colonic ulceration. Sigmoidoscopy is an essential procedure and despite considerable observer variation,<sup>1</sup> it usually provides a firm diagnosis. Unless the patient has some infirmity that prevents, this is best done in the knee-elbow position. A standard 25 cm instrument is used. A preoperative enema is rarely necessary. It is wise to obtain the patient's consent to a mucosal biopsy in advance, so that if the conditions observed in the rectum or colon are not clear-cut, a specimen may be obtained for histological examination.

A plain film of the abdomen should always be taken before a barium enema is done. Since it is the only method of visualizing the whole colon, barium enema studies should be carried out in all cases except those in which the patient is too ill. If the terminal ileum is not filled by the contrast medium, a small bowel series should be done later, to exclude the possibility of granulomatous disease involving both small and large bowel. Opinion varies as to suitable preparation for barium enema. In ulcerative colitis we do not use even a small dose of castor oil as preparation. If retained fecal matter is likely to be present a simple warm water enema should be used.

In acutely ill patients with colonic dilatation, plain abdominal x-ray films will usually give all the necessary information and barium enema may be postponed until the patient's condition improves; the enema procedure is then safer and better tolerated. Although some textbooks still advocate adding tannic acid to the barium mixture to inhibit mucus secretion and increase muscle contraction, studies have shown unequivocally that this once largely used agent is hepatotoxic and should not be given in any circumstances.

Experience suggests that there is a tendency to exaggerate the importance of the radiological appearances of the colon in prognostication. Loss of haustral configuration is certainly reversible, and often changes that are at first taken to represent fibrous strictures are shown in retrospect to have been due to local muscle spasm. True strictures are indeed rather rare; but if what appears to be a stricture persists, carcinoma must be suspected until completely excluded. Serious doubts may have to be resolved by laparotomy, but fortunately this is rarely necessary. Other conditions to be considered in the differential diagnosis of ulcerative colitis are regional enteritis or Crohn's disease of the colon (which is often associated with

disease of the small intestine), amebic colitis, vascular occlusive disease of the bowel and, rarely, colonic manifestations of systemic connective tissue disease. Rectal biopsy usually, but not always, provides incontrovertible proof of the diagnosis.

## Complications of Ulcerative Colitis

*Local complications.* In both the acute attack and in the chronic disease local complications in and around the rectum and anus may occur. Bleeding hemorrhoids are quite common. They may precede the ulcerative colitis, and rectal bleeding, when it occurs as the first symptom of colitis, may be ascribed to them, or they may result from or complicate tenesmus associated with the disease. Ischio-rectal abscess, fistula-in-ano and recto-vaginal fistula occur, sometimes as the presenting or as early features of the disease; however, with the increasing recognition of granulomatous colitis (Crohn's disease of the colon), which will be discussed later, it seems that these complications are commoner and more intensive in granulomatous disease than in ulcerative colitis. They are also less amenable to treatment.

Massive hemorrhage from the colon is rare but may be dangerous. Perforation of the colon during an acute attack is a rare but highly dangerous complication. It involves most frequently the sigmoid or descending colon. It may be overlooked until widespread peritonitis has developed. It may sometimes be preceded by acute and pronounced dilatation of part or all of the colon. Hence this dilatation is deemed a bad prognostic factor. However, it is likely that there is no single cause of this dilatation and that the terms *toxic megacolon* and *toxic aganglionosis*, which have been applied to it, imply unwarranted assumptions about causation. Severe mucosal disease, the use of anti-cholinergic drugs and electrolyte imbalance may each play a part, and true aganglionosis has not been demonstrated.

Finally, and most important, there is the risk of colonic carcinoma in ulcerative colitis. Published data show a higher incidence than in a healthy population, but the extra risk is hard to evaluate. Data on surgical series have tended to show a higher incidence than have data on non-surgical series. The highest risk occurs in patients in the younger age group in whom the initial attack is severe, the whole colon is involved and a complete remission has not been obtained. In such patients the incidence of colonic carcinoma may be as high

as 20 per cent within 20 years. The incidence for all cases of ulcerative colitis is about 3.5 per cent and is about seven times that in the population at large, according to Edwards and Truelove.<sup>6</sup> Up to seven years after the first attack the incidence was only 0.5 per cent. Over the next seven years the cumulative risk, calculated actuarially, was 1.6 per cent. After this time the risk rose sharply. The carcinomas may be multifocal and they are more evenly distributed than in colonic carcinoma arising *de novo*. The apparently worse prognosis associated with such growths may be due in part to an absence of warning symptoms when the colitis is symptomatic and also to the fact that many of the growths are beyond the reach of the sigmoidoscope. In any relapse or deterioration in ulcerative colitis, carcinoma should be suspected and, if increased therapy is ineffective, examination with barium enema should be done.

*Extraintestinal complications.*<sup>5</sup> A considerable variety of skin lesions may occur in ulcerative colitis. They may be mild and transient, or lesions typical of erythema nodosum and erythema multiforme may occur. A more specific but rare complication is pyoderma gangrenosum; this is associated with severe disease in the main and may be localized or spread to produce severe and widespread skin destruction, occasionally being the determinative factor in decision to do colectomy.

Severe acne or pustular dermatitis may occur spontaneously or in association with corticosteroid therapy, and use of azulfidine may also produce rashes of protean types. In the mouth aphthous ulcers are common, and sometimes, in severe ulcerative colitis, similar lesions may involve the esophagus. Ocular complications, conjunctivitis and iritis, appear quite often. Arthralgias are probably the commonest complications of ulcerative colitis. Large joints such as the hips, knees and ankles are most commonly affected, but small joints also may be affected and the symptoms may resemble those of rheumatoid arthritis. However the Rose-Waaler test is usually negative<sup>3</sup> and the joint symptoms usually abate with remission of colitis or on colectomy. Pain and stiffness and moderate swelling occur, but since joint destruction is rather uncommon the joint disease generally is reversible and, where it is not, the possibility of coincidental rheumatoid arthritis must be entertained. Spondylitis shows the same high incidence, some 20 to 50 times that in a general hospital population.

There is no agreement about the type of liver disease associated with ulcerative colitis. At the Mayo Clinic much emphasis has been placed recently on the association of pericholangitis with colitis.<sup>17</sup> Obstructive hepatic disease with elevated serum alkaline phosphatase activity was the distinctive feature. Mackay in Melbourne has emphasized a "lupoid" type of hepatitis; other investigators have merely noted a high incidence of fatty liver. A recent study from Chicago<sup>14</sup> has shown that cirrhosis is 12 times as common in ulcerative colitis as in a control population and it is now apparent that liver disease probably does have more importance in ulcerative colitis than has been suspected in the past and that well designed prospective studies are needed to determine whether the risk of irreversible liver disease should influence the treatment of ulcerative colitis. The same comments apply to renal disease associated with ulcerative colitis. The incidence of pyelonephritis may be significantly raised. Urinary calculi, too, may be a significant complication, although the published data do not establish this satisfactorily.

## Treatment

*General Measures.* In the majority of cases, treatment is by conservative means; but in perhaps one or two per cent of all cases of acute ulcerative colitis early colectomy is necessary. The decision to operate is not difficult if perforation or massive colonic hemorrhage or severe dilatation occurs. The real difficulty is to decide when a patient without any of these complications is nevertheless too sick to respond to conservative treatment, and delaying colectomy may endanger life. The mortality associated with emergency operation is high.

Part of the medical treatment of the moderately severe or severe attack is that used in any case of acute, bloody diarrhea—namely, hospitalization, restoration of fluid and electrolyte balance, if necessary by intravenous infusion, blood transfusion if anemia is present and a highly nutritious and appropriate diet, from which spices, irritants such as coffee and citrus juices and coarse fibres are excluded. The patient may require sedation with phenobarbital. Broad spectrum antibiotics must not be used and anticholinergic drugs are best avoided. To correct the iron deficiency anemia that frequently is associated with attacks of ulcerative colitis, iron preparations should be given intramuscularly, not by mouth.



*Special Therapeutic Regimens.* The lesson learned from numerous controlled trials is that patients with all but the mildest degrees of the disease should be treated with systemic steroids, 40 to 60 mg of prednisone daily for adults. This is combined with topical steroids, 100 mg of hydrocortisone hemisuccinate in 100 to 200 ml of saline solution by enema once or twice daily, and 4 to 8 gm of azulfidine daily divided into four doses. If the patient is very sick, then the prednisone is given intravenously as prednisolone 21-phosphate, 40 mg daily, by intravenous drip, which also serves to control water and electrolyte imbalance. When the expected response occurs, the dosage of systemic steroid is discontinued by stages after 2 to 3 weeks, with the topical hydrocortisone and the azulfidine continued until the sigmoidoscopic appearances are normal. The topical treatment is then discontinued, but azulfidine is continued indefinitely but with the dose reduced to 2 gm daily, since a controlled trial has shown that such treatment significantly reduces the incidence of relapse.

Rectal biopsy is the most sensitive measure of complete remission and is a valuable guide to therapy, but clinical and sigmoidoscopic findings usually provide adequate indices of the state of the disease. We examine patients, including sigmoidoscopic examination, at intervals of two weeks and then of four weeks for the first few months. In mild first attacks and relapses we use topical hydrocortisone and oral azulfidine, discontinuing the hydrocortisone after a remission has been achieved. If the disease is mild and limited to the rectum, prednisone suppositories alone, used once or twice daily, are effective; but if a response does not occur within a week, we start treatment with hydrocortisone enemas and azulfidine. Many of these patients can safely continue their ordinary activities.

A few patients with chronic ulcerative colitis have relapse each time steroids are discontinued. Continuous therapy is frequently used in such patients but there is always risk of acute exacerbations despite therapy. Also complications may arise from steroid treatment, and the expense may be considerable. It is in patients of this group that hypercortisonism most frequently occurs, with cushingoid features and sometimes irreversible damage to the skeleton. The majority of these patients ultimately come to colectomy and ileostomy and are then cured of the disease. With

experience, a physician may be able to recognize patients of this type fairly early, but prognostic errors cannot be completely overcome.

At present we are trying to evaluate continuing medical supervision and treatment of patients who have had moderate and severe attacks of ulcerative colitis and have responded to therapy. Recurrent attacks are the rule in this disease and each attack carries a risk to the patient. Treatment of an attack may be long and expensive. There is a later risk of cancer, especially in young patients with extensive disease of the colon in whom remissions are short-lived or incomplete. Since the risk of dying within 20 years of the first attack is greater than in a comparable group of normal subjects, colectomy and ileostomy may be the treatment of choice in patients who have frequent relapse. There are no hard and fast rules. After the physician has become familiar with that patient's disease pattern and temperament, he will have to decide between conservative treatment and recommending operation. At present about 20 per cent of all patients are operated upon, but with earlier effective medical treatment and careful follow-up in remission this figure could probably be halved.

Recently we have been doing ileostomy in a number of cases, with retention of the colon, and treating the patient with the full medical regimen including both systemic and local use of corticosteroids after diversion of the fecal stream. It was hoped that in some of these patients intestinal continuity could be restored later when the colon had returned to normal, and that other patients, if colectomy finally became necessary, would by that time be far better prepared for it psychologically than if a colectomy were done as a first surgical procedure. To date, our limited experience and that of other observers<sup>20</sup> suggests that improvement is disappointing (unlike that seen in granulomatous colitis, which will be discussed later) and that ileostomy of this type does not have any application to most patients with ulcerative colitis.

Complications that can come from the use of corticosteroids and azulfidine must be borne in mind. Some of those associated with corticosteroids have possibly been overemphasized; they may be complications of the disease and not of the therapy. However, during therapy with this agent infections may be masked and tuberculosis reactivated. Monilial infections seem to occur more

frequently and in more severe a form. Rarely, perforation of a viscus may occur relatively asymptotically. Peptic ulceration is rare, but a previous history of peptic disease must be regarded as a factor in planning treatment. Mental symptoms of insomnia and hypomania seem to be more common and may necessitate the reduction of dosage with corticosteroids. Some surgeons have the impression that patients who have been treated with corticosteroids for any length of time before operation have an extraordinarily high incidence of postoperative complications, but formal analysis of data does not support that impression.<sup>8,10</sup> Provided proper corticosteroid and antibiotic cover is given during and after operation, no untoward results should occur. Treatment with azulfidine is frequently associated with headache, nausea, rashes and neutropenia. Heinz-body hemolytic anemia sometimes occurs. Our experience, however, has suggested that when steroids are given concomitantly with azulfidine, these side effects are much reduced. Only rarely are they of a degree to impose reduction of dosage or discontinuance of the drug.

### Psychotherapy

The role of psychotherapy in the management of ulcerative colitis is still debatable. Recent reports of a prospective long-term controlled clinical study suggest that psychotherapy emphasizing the analytical approach confers a definite advantage.<sup>13</sup> There has been, however, no comparison of psychotherapy by internist and by psychiatrist. Lacking such data, my opinion is that the whole care of these patients is best conducted by the internist, who should be able to provide adequate psychotherapy except in the uncommon cases of frank psychosis. Analytical probing during an acute attack is probably always harmful, since the patient is too ill to face up to such a confrontation; he may become withdrawn and uncooperative as a result. Psychotherapy may be instituted when the disease is mild or in remission and if the patient requests it.

### Diet

Exclusion of certain foods has been widely advocated, usually in a rather unsystematic way. Indeed, the first properly conceived and executed trial of specific dietary exclusion of cow's milk protein in ulcerative colitis has only been reported in the past year.<sup>21</sup> About 15 per cent of patients

in this trial showed a favorable response. The need is evident for similar studies, excluding other foods which have been held to be culpable, such as eggs, nuts and tomatoes. Without such studies there is a good case for properly conducted trials of elimination diets in patients usually refractory to standard treatment or who have frequent relapse. Unfortunately no laboratory tests or tests of skin-sensitivity have proved to be of established value in predicting response to specific exclusions of foods.

### Surgical Treatment

In the management of ulcerative colitis internist and surgeon should work together. In this way the understanding of the various problems of the disease by both is much enhanced, to the benefit of the patient. Surgical treatment may be minor and involve only drainage of an ischiorectal abscess, excision of an anal fissure or the laying open of a fistula. In acute attacks the operation—if operation is necessary—is essentially colectomy, which must be performed for the complications mentioned above. In patients with chronic ulcerative colitis for whom adequate remission cannot be obtained or who have frequent recurrences, radical operation—total colectomy with removal of the rectum—may be necessary. This is the most widely accepted treatment but a few surgeons attempt to preserve the rectum, doing an ileorectal anastomosis to preserve normal defecation. This has been much criticized recently on the ground that the risk of carcinoma in unremitting disease involving the whole colon is very high and the rectal stump is as liable to neoplastic change as any other segment of the large bowel. However, in patients who have extreme fear or dislike of ileostomy the more conservative operation is justifiable and frequent routine proctoscopic examination will lessen the risk. It must be emphasized that the postoperative course may be complicated by rupture of the anastomotic junction. Also chronic proctitis may occur and the patient may pass frequent soft stools.

An important point arises when any operation is planned in patients with ulcerative colitis who are being treated or recently have been treated with corticosteroids. Substantial doses of soluble corticosteroid must be given during operation and in the early post-operative days. We have used hydrocortisone hemisuccinate 100 mg every 8 to 12 hours throughout this period.



## Treatment of Complications

Such local complications as ischio-rectal abscess, fistula-in-ano and anal fissure are treated by drainage and appropriate conservative operation, unless the lesions are so extensive that colectomy is indicated. Temporary diversion by ileostomy may be valuable in such cases. Perforation demands emergency colectomy. Although most internists experienced in the disease have brought patients with acute colonic dilatation into remission on medical treatment, this demands constant surveillance, some anxiety and a risk of perforation which will much increase the chances of the patient's death. In these circumstances few would argue against emergency colectomy.

Polyposis of the colon demands continuing observation. Colonic stricture usually responds well to segmental resection when the disease has become quiescent. The remote complications of the disease respond almost always when the colon responds to treatment. Sometimes arthritis, eye complications or pyoderma gangrenosum may be so severe that colectomy has to be performed on their account. These complications usually then promptly abate.

## Long-term Management

Patients with ulcerative colitis in remission are instructed to report immediately if even minor symptoms recur, so that vigorous therapy can be started early in the relapse. Intercurrent infections seem to increase the risk of relapse, and patients are warned to reduce their activities and even take to their beds for a day or two if upper respiratory infections or influenza develop. Many patients become aware of certain emotional or environmental factors which are associated with relapse, and learn how to avoid them. If an exclusion diet has been used, it must be maintained indefinitely.

Azulfidine in a dose of 2 gm daily has been shown by controlled trials to reduce significantly the incidence of relapse. It is now used routinely except in patients who have unpleasant side effects from the drug.<sup>12</sup>

Recent data suggest that the incidence of colonic carcinoma is sufficiently high to warrant a barium enema examination every six months in young people and rather less frequently in older patients.

## Ulcerative Colitis and Regional Enteritis

It is appropriate here to consider a cause of chronic ulcerative disease of the colon which has only been emphasized in the past five years and which has been separated from ulcerative colitis by clinical, pathological and radiological criteria. We usually think of regional enteritis as a disease quite distinct from ulcerative colitis. It involves classically the terminal small intestine, the lesions consisting of thickening, with hyperplastic change in the intestinal wall, fibrosis, the formation of strictures and of fistulae. In the active phases of the disease there is pronounced enlargement of regional lymph nodes. Microscopically, the pathognomonic lesion is the non-caseating granuloma, consisting of epithelioid and giant cells. These lesions are found especially in the submucosa, where the disease is thought to begin. But they are also present in the muscle layers and sometimes in the regional lymph nodes.

In ulcerative colitis the disease is virtually limited to the colon, the earliest inflammatory changes occur in the lamina propria of the mucosa, and the lesion thought by many to be most typical of the disease is the crypt abscess. However, over the last few years the observations of Morson and his colleagues in London and of the group at the Mount Sinai Hospital in New York have established that the lesions of granulomatous colitis or Crohn's disease of the large intestine may occur both in the absence and in the presence of lesions elsewhere in the intestinal tract. Morson particularly has emphasized the much higher incidence of anal lesions, especially fistulae and fissures, associated with the granulomatous disease than with ulcerative colitis.

The same spectrum of extra-intestinal complications may be found in this condition. When the rectal mucosa is involved the appearances are different from those seen in typical ulcerative colitis, in that, if ulceration is present, the mucosa between areas of ulceration appears normal and very often the same cobblestone appearance of the mucosa can be seen by naked eye as may be seen elsewhere in the colon on radiological examinations. Radiologists have emphasized this cobblestoning and the presence of deep linear fissures in the mucosa in Crohn's disease of the colon. With experience, it is possible to distinguish between the two conditions on radiological grounds. Should any doubt persist, biopsy of the rectal mucosa may resolve the problem, although it

does not always do so. This distinction between ulcerative colitis and regional enteritis of the colon is not an academic one, since it becomes increasingly clear that whereas the risk of carcinoma of the colon is high in ulcerative colitis, in regional enteritis it is slight. Further, deviation of the fecal stream from the colon in granulomatous colitis has proved far more successful in our experience than it has in ulcerative colitis. The main differences are summarized in Table 1, which is based on Morson's studies.

Whether these two conditions have different etiologic lineage is quite undecided. We know little of the causes of either condition and it is possible that the difference in the pathologic changes are merely due to differences in tissue response to similar or identical traumatic factors. It is noteworthy that, in some reported cases, features of both ulcerative colitis and of regional enteritis were observed; also that in some families some of the members will have one of the diseases, other members the other. In some cases ulcerative colitis is reported to have evolved into regional enteritis.

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TABLE 1.—*Main Differences Between Ulcerative Colitis and Crohn's Disease of the Colon*

	Ulcerative Colitis	Crohn's Disease
Symptoms.....	Mild pain, rarely severe Bleeding almost invariable Often frank blood Severe anal lesions uncommon	Severe cramps in many Bleeding in less than half Frank blood uncommon Severe anal lesions common
Sigmoidoscopic appearance.....	Mucosa uniformly involved  Rectum involved in 95 per cent of cases	Circumscribed lesions—cobblestones. Intervening mucosa may be normal Rectum frequently spared
Radiological attributes.....	Disease continuous Rectum rarely spared Diffuse ulceration Pseudopolyps Back-wash ileitis with ileal dilatation  No internal fistulae	Disease segmental Rectum often spared Deep fissures Cobblestone appearance Narrowing and abnormal mucosal pattern of terminal ileum Fistulae may occur



# Report of the SCIENTIFIC BOARD

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## Coronary Care Units

CORONARY ARTERY DISEASE has been the leading single cause of death for many years. More than 500,000 persons died of it in 1964. Preventive measures and improved treatment and diagnosis have not greatly lowered the mortality rate. A most encouraging development has been the establishment of coronary care units, as described by Day,<sup>1</sup> and amplified by others.<sup>2,3,4</sup> Recently published reports from the coronary care units in Bethany\* and Presbyterian† hospitals show a mortality from myocardial infarctions of approximately 19 per cent as compared with 28 to 30 per cent in patients receiving conventional hospital care.<sup>1,2,5</sup>

There is a rapidly increasing amount of information on the arrangements and equipment necessary for coronary care units, but the most essential element for a successful unit in a hospital is a coronary care committee composed of physicians, nurses, administrators and medical technical staff personnel. The committee should study available literature on this subject, consult with local authoritative sources such as might be provided by the Heart Association or the Medical Society, visit existing operating coronary care units and finally, plan and establish a set of policies applicable to its particular hospital.<sup>6,7</sup> If new construction is neces-

sary, an architect should be included in the planning committee, either as a member or as a consultant.

The committee would be responsible for recommendations on (1) the selection of personnel for the unit, (2) medical staff decisions relevant to care to be provided in the unit and (3) physical arrangements and equipment. These will vary with the local medical customs, size of the hospital and resources available. Much information on these items can be found in the references listed below. Certainly no medical staff should begin a unit without a clear understanding of these facts, and careful review of the evidence, the problems, and the cost of a coronary care unit.

Next in importance to careful planning by the committee is training of all of the physicians and hospital personnel who will be using or working in the coronary care units.<sup>3,5,8</sup> The nurse must be adequately trained in handling emergency situations, be capable of identifying cardiac arrhythmias, and be given specific authority to institute therapy. It is to be emphasized that this approach appears particularly necessary in hospitals where it is impossible to have a physician on duty all of the time. This does not negate the physician's role, but emphasizes the nurse's role as a trained emergency technician. Unless the nurse is trained to fulfill the above functions, and authorized to do so, the full advantage of a coronary care unit will not be realized. Not all of the medical-legal aspects have been clarified, but the Council of the California Medical Association has approved a statement on this prepared by the Committee on Other Professions of the California Medical Association.

Although coronary care units in this country have been established for only a relatively short

This statement was prepared by Stanford S. Kroopf, M.D., Chairman of the project Committee on Coronary Care Units, California Heart Association, the Committee on Scientific Information of the Scientific Board.

Editor's note: See joint statement by the California Medical Association, the California Hospital Association and the California Nurses' Association on the Role of the Registered Nurse in Acute Coronary Care, page 228.

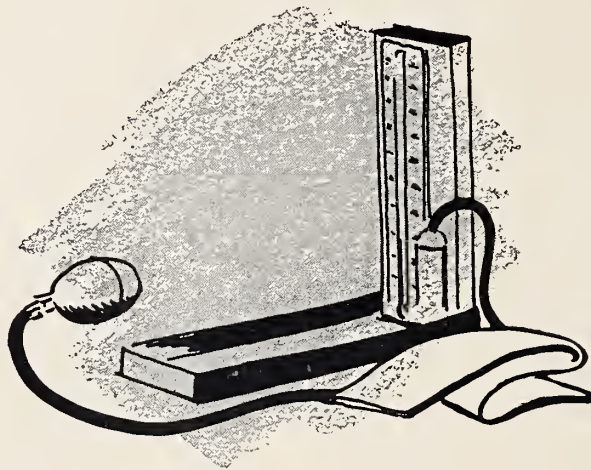
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†Philadelphia.

period of time, the reports on these units have been very promising. Further research and performance records from many more such units are needed to demonstrate statistically their effect on the mortality rate from acute myocardial infarctions.

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# CASE REPORTS

## Acute Renal Tubular Necrosis Due to Water Intoxication

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TOXIC NEPHROPATHY may be caused by a variety of agents and conditions.<sup>7</sup> These may include metals, solvents, chemicals used in diagnostic procedures, abnormal concentrations of physiological substances, or physical insults to the body economy such as excessive water intake in a hot climate. In the case reported here the condition was due to excessive water intake, no salt and 12 hours of desert sun.

A healthy adult not sweating immoderately would require about two liters of water a day,<sup>4</sup> and ingestion of huge amounts of water without concomitant increase in electrolytes can dangerously upset the normal body values of 2,700 to 3,000 milliequivalents of sodium and about 3,000 milliequivalents of potassium. For disturbances of this order, a new classification (N981.5)\* will soon be provided.<sup>6</sup>

A minimum of sophisticated laboratory procedures are needed to measure the gravity of situations of this kind,<sup>2,5</sup> but serial determinations of creatinine and urea nitrogen values and of serum and urine sodium contents are needed as a guide for effective therapy.

### Report of a Case

A husky 57-year-old white border patrol officer who had worked all day in a desert area with air temperatures averaging 110°F, collapsed at sunset and was admitted to hospital where his tempera-

ture was reported to be 103°F. It was learned that during the day he had drunk more than two gallons of unsalted ice tea, and ice water. For years he had omitted milk, milk products and salty foods from his diet. A series of convulsions occurred in the 24 hours following admission, apparently precipitated by intravenous infusion of 2 liters of 5 per cent dextrose in water. Violent agitation required maximum restraint. In the second 24 hours he passed almost no urine. He was transferred to Donald N. Sharp Memorial Hospital by ambulance 48 hours after the heat exposure.

On admission he was disoriented, almost anuric and acutely ill. Deep abrasions were present on the wrists and ankles from restraint cuffs. Body temperature was 99°F, the pulse was full and bounding at a rate of 100 to 120, respirations 26 to 30 per minute and blood pressure 210/100 mm of mercury.

A retention catheter was placed and the output of urine in the first 24 hours was 625 ml. The urine (with a specific gravity of 1.010) contained 1.750 gm of albumin per 100 ml and a trace of glucose. Leukocytes numbered 20 to 40 per high power field and each field was filled with erythrocytes. Blood urea nitrogen was 61 mg and blood sugar 100 mg per 100 ml. Serum cholesterol was 123 mg per 100 ml. Hemoglobin content was 12.1 gm per 100 ml of peripheral blood, the hematocrit was 37 per cent, and leukocytes numbered 14,470 per cu mm with 76 per cent polymorphonuclear neutrophils. The spinal fluid pressure was within normal range and the fluid contained 3 leukocytes (all neutrophils) per field. A Pandy test for globulin was negative. The sugar content was 67 mg and protein content 17 mg per 100 ml of fluid. A Kolmer test was non-reactive.

The condition of the patient deteriorated the following day, and psychiatric consultation suggested a chronic brain syndrome should be considered. An electroencephalogram was reported

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\*In the World Health Organization's Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death.

as showing moderate generalized paroxysmal dysrhythmia suggesting diffuse central nervous system disease. (About four years previously the patient had had an electroencephalogram that was entirely within normal limits.) A urological consultant believed acute tubular degeneration without obstructive uropathy to be present, and the following day an internist consultant reached the same conclusion.

Intensive supportive care was given but three days after admission the blood urea nitrogen had risen to 80 mg per 100 ml. Serum creatinine was 12 mg per 100 ml, and serum sodium and potassium 121 and 5.5 mEq per liter respectively. Excretion of phenolsulphthalein was 4 per cent in two hours. Urine sodium was reported to be 19 mEq per liter. This value rose to only 20 mEq the following day.

Four days after hospital admission, sodium and potassium levels had returned to normal, and all vital signs including blood pressure were within normal limits, but the blood urea nitrogen was 112 mg and serum creatinine 12 mg per 100 ml.

Beginning 48 hours after admission mannitol was given intravenously, 50 gm daily was used to promote diuresis,<sup>3</sup> with salutary effect (Table 1). Administration was discontinued after four days when fluid output began exceeding intake.

Urine chlorides remained very low (20 and 26 milliequivalents per liter on the fifth and sixth days in hospital) but the sensorium cleared dramatically with diuresis. Blood pH four days after admission was 7.42 with a base excess of -7. Dialysis was not performed. Radiographs of the lungs on the fifth day showed only a small amount of pleural fluid at the left base.

Body weight declined from 210 pounds when the patient was admitted to 199 pounds when he was discharged seven days later.

Two weeks after discharge all vital signs were

normal, the sensorium was clear, blood urea nitrogen was 15 mg and serum creatinine 1.1 mg per 100 ml, and results of a blood cell count and urinalysis were entirely within normal limits, as were serum, sodium, potassium and chloride. On neurological examination no abnormalities were noted.

## Summary

A 57-year-old white man with acute tubular necrosis that had developed from excessive water drinking while working in a hot desert area, had alarming mental and physical symptoms.

Gratifying recovery followed conservative treatment. Administration of large amounts of mannitol intravenously—as recommended by Barry and coworkers<sup>1</sup>—contributed to this good result.

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## Surgical Treatment of Massive Pulmonary Embolism

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MASSIVE PULMONARY EMBOLISM is almost always a fatal disorder.<sup>7,10</sup> In 1908 Trendelenburg<sup>21</sup> asked "whether the diagnosis of embolism can be ascertained with sufficient accuracy and whether there

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TABLE 1.—Data Showing Diuretic Effect of Mannitol Intravenously, 50 gm a Day (Asterisks Indicate Days of Mannitol Therapy)

Date Admitted	Body Weight (pounds)	Fluid	
		Intake (milliliters)	Output
5-2-65.....	210	2,850	200
5-3-65.....	208	3,850	625
*5-4-65.....	207	2,700	1,600
*5-5-65.....	205	2,675	2,385
*5-6-65.....	203	2,940	2,660
*5-7-65.....	202	2,390	3,800
5-8-65.....	201	2,645	4,100
5-9-65.....	199	2,100	3,425



is sufficient time for an operation." Subsequently he attempted surgical removal of pulmonary emboli in three cases without success. In 1924 Kirschner<sup>13</sup> performed the first successful Trendelenburg operation. Between then and 1961, when Cooley<sup>4</sup> reported successful removal of a massive pulmonary embolus while the patient was sustained with cardiopulmonary bypass, the total of successful operations rose to only 23. Then in less than three years an additional 18 patients were salvaged with this procedure. Now, with the perfection of techniques for cardiopulmonary bypass in many medical centers, Trendelenburg's query becomes much more pertinent.

### Feasibility of Pulmonary Embolectomy

Donaldson<sup>3</sup> reviewed 283 cases of pulmonary embolus, proved at autopsy, which occurred on the Massachusetts General Hospital Surgical Services over a 30-year period. In 271 cases, the time interval could be determined. Twenty-five per cent of this group survived longer than one hour, 22 per cent longer than two hours and 17 per cent longer than six hours after onset of embolism. An analysis of 52 autopsy proven cases of pulmonary embolism by Flemming<sup>9</sup> demonstrated a 55 per cent two-hour survival and a 48 per cent eight-hour survival in patients who were previously healthy. These studies certainly indicate that there is adequate time to ready cardiopulmonary bypass for pulmonary embolectomy in many patients with pulmonary embolism and underscore the need for expeditious diagnosis of this disorder.

### Reports of Cases

Recent experience with successful pulmonary embolectomy in two cases at Santa Clara County Hospital serves to illustrate several features concerning the diagnosis, decision to operate, surgical problems and postoperative morbidity associated with this procedure.

**CASE 1.** A 29-year-old Caucasian mother of four had vaginal hysterectomy at Campbell Community Hospital, 29 October 1964. At 1 p.m. on the fourth postoperative day, she began having severe pleuritic substernal pain, pronounced dyspnea, occasional non-productive cough and tachycardia of 120. A few rhonchi were heard in the left lower lung field. A film of the chest was within normal limits. At 4 p.m. excruciating chest pain began abruptly, accompanied by vomiting and signs of shock. Pronounced cervical vein dis-

tention was noted, a widely split aortic second sound, pulsus paradoxicus, protodiastolic gallop rhythm and moderate agitation. An electrocardiogram indicated right heart strain.

The patient was then treated with metaraminol, digitalis, heparin and oxygen. She had persistent hypotension and intractable chest pain over the next few hours. Eventually norepinephrine was begun to maintain arterial blood pressure and an electrocardiogram was consistent with incomplete right bundle branch block.

The patient was admitted to Santa Clara County Hospital 2 November 1964 at 11 p.m. On physical examination the findings already mentioned were noted, plus non-tender abdomen, non-tender extremities, shallow respirations, clear breath sounds and a pulse rate of 160. She was taken directly to the operating room where, after cannulation of the right femoral vein and right femoral artery under 1 per cent lidocaine anesthesia, partial cardiopulmonary bypass was begun. A disposable bag oxygenator was used and primed with Ringer's lactate and two units of heparinized ACD blood. The patient remained alert and talkative, but had a sensation of impending doom throughout these preparations. General anesthesia was then induced with halothane via endotracheal tube, and median sternotomy was done. The vena cavae were cannulated via the right atrium and total cardiopulmonary bypass at a flow rate of 3,300 ml per minute was begun.

A longitudinal main pulmonary arteriotomy was performed, and upon opening the lumen a grapelike mass was immediately extruded. Additional clots were then removed from both main pulmonary arteries and their major branches. The lungs were then milked bilaterally and more clot material was removed. The arterial incision was sutured and the bypass was discontinued after 20 minutes of total bypass time. The lumbar vena cava was then doubly ligated with 0 silk ligatures via a flank incision.

Examination in the immediate postoperative period showed normal heart sounds, no conduction defect in the electrocardiogram and no cervical vein distention. The postoperative course was complicated by a right hemothorax which developed one week following embolectomy and required decortication on the 18th postoperative day. The patient was also bothered considerably by phlebitis in the right leg. Moderate swelling of the right lower extremity persists to the

present time but she has returned to her duties as a housewife.

**CASE 2.** A 54-year-old Caucasian man, a painter, was first seen at Santa Clara County Hospital in December 1964 with complaint of sudden onset of numbness, parasthesias and cyanosis of the fingers of the left hand. After extensive diagnostic study of this neurovascular disorder, left cervical sympathectomy was done 18 January 1965 through a right thoracotomy in the third intercostal space. After moderate ambulation on the second postoperative day, the patient had pain in the left side of the chest. On examination this was difficult to distinguish from wound pain. An electrocardiogram suggested minor ischemic changes. The following morning the patient was apprehensive but his blood pressure was stable and the pulse rate was under 100. At 1:15 p.m. on the third postoperative day, pronounced dyspnea and signs of shock developed. Although the patient had no significant chest pain, he had a sensation of pressure on his chest.

Blood pressure and pulse were briefly unobtainable; but soon a pressure of 56/0 mm of mercury developed with a pulsus paradoxicus and the patient remained responsive at all times. His skin was decidedly violaceous. On auscultation a protodiastolic gallop rhythm with a fixed split of the second heart sound was noted. An electrocardiogram taken at this time indicated complete right bundle branch block, which had not been present on a tracing 24 hours before. The circulation time was greater than one minute.

An attempt to document the diagnosis of pulmonary embolus was made in the radiology department with bilateral cephalic vein infusion of large amounts of sodium diatrizoate. Films taken from 45 to 90 seconds after infusion showed no dye material in the superior vena cava. The patient was taken immediately to the operating room, where preparations for cardiopulmonary bypass had been made. Under local 1 per cent lidocaine anesthesia, cannula was put into the right femoral artery and a large plastic cannula was placed in the right internal jugular vein. Partial bypass was established at a flow rate of 2,000 ml per minute. A few minutes later, the patient lost all evidence of pulsatile flow and the systemic arterial systolic pressure was 50 mm of mercury while the venous pressure was 20 mm of water. The pump flow was gradually increased to 3,000 ml per minute and general anesthesia

with halothane via endotracheal tube was begun. At this instant, the systolic arterial pressure was 25 mm of mercury. As soon as the sternum was opened and the right atrium cannulated, the systolic arterial pressure rose to 80 mm of mercury, pulsatile flow returned and the vital signs stabilized.

Total bypass then was begun and a longitudinal incision was made in the main pulmonary artery after cross-clamping of the trunk. The lumen of the right pulmonary artery was found to be totally occluded with clotted material. An embolus 18 cm long and 1 to 1.5 cm in diameter was removed in one piece. Several other small clots were removed. No clotted material was found in the left main pulmonary artery. Both lungs were milked and peripheral clots were recovered only from the right side. Bypass was discontinued approximately one hour after it was begun.

During the closure of the thoracic wound and ligation of the abdominal vena cava, the patient had two episodes of atrial flutter with block. The heart reverted to normal sinus rhythm spontaneously.

On physical examination in the immediate postoperative period, heart sounds were normal, there was total reversion of the right bundle branch block to normal sinus rhythm, and neck vein distention disappeared. The patient was hampered in the postoperative period with edema of both legs but there was no evidence at any time of acute thrombophlebitis. Anticoagulant therapy was begun on the seventh postoperative day. When last examined the patient could tolerate moderate exercise without leg edema.

## Discussion

Because of the limited survival time in patients with pulmonary embolism, an attempt should be made to establish necessary criteria for a confident diagnosis on clinical grounds alone, lest valuable time be lost.

The diagnostic features in the cases reported here included:

- Abrupt development of clinical shock.
- Evidence on physical examination of right ventricular overload and dilatation.
- Systemic venous congestion without signs of pulmonary venous congestion.
- An electrocardiogram characteristic of acute right heart strain.



- No previous significant heart disease.
- Pulsus paradoxicus.

The sudden development of tachycardia and hypotension with peripheral signs of shock occurred in both cases. In the first case, sustained use of vasopressors became necessary, but eventually these were to no avail. In the second case, a vasopressor was used for the first hour and then adequate blood pressure was maintained without drugs in the interval before operation. Signs of pronounced peripheral vasoconstriction persisted in both cases, but both patients remained amazingly alert until induction of general anesthesia.

The presence of a heave and a protodiastolic gallop at the lower left sternal border reflected the dilatation and overload of the right ventricle. In both cases, the second heart sound was found widely split and fixed with respirations and the sound of pulmonic valve closure was prominent.<sup>2</sup> At this time the electrocardiogram in both cases demonstrated a right bundle branch block. The electrical delay in right ventricular activation as well as mechanical prolongation of the right ventricular systolic ejection were the likely explanations for the wide separation found between aortic and pulmonic closures, but the fixation of the interval with the respiratory cycle requires further explanation.<sup>12</sup> Perhaps the extreme distention of the right ventricle in diastole made the chamber non-compliant and it was unable to change significantly in end diastolic volume with the fluctuation of intrapleural pressure. Hence, the usual increased filling of the right ventricle during inspiration did not occur. In both cases this chamber was observed at operation to be tense and distended during diastole. In both cases also the abnormal second heart sound reverted to normal shortly after removal of the pulmonary emboli.

Abnormal cervical vein distention was quite obvious in both cases. The patient in Case 1 was decidedly orthopneic but pulmonary rales did not develop. The other patient was quite comfortable in the supine position throughout his preoperative course and had clear breath sounds. As McGinn<sup>16</sup> noted in his series of autopsy-proven cases, the patient with a massive embolism has pronounced systemic venous congestion in the absence of pulmonary congestion.

Electrocardiograms were helpful in the diagnosis in both cases. In the first tracings made after development of symptoms, a right ventricu-

lar conduction delay was found. In Case 1 this was classified as an incomplete right bundle branch block for the QRS duration measured 0.10 seconds. The QRS axis was 90° in the frontal plane and a slurred monophasic R wave was present in lead VI. An electrocardiogram taken one week after embolectomy showed a normal QRS duration of .08 second, an rS pattern in lead VI and a QRS axis of 60°. In the second case, a complete right bundle branch block was found at the onset of shock. This was noted to return to normal within two hours after pulmonary embolectomy was completed.

Further confidence in the clinical diagnosis was afforded by the fact that neither patient had a history of any previous cardiac disease. This information aided in distinguishing the acute episode from chronic pulmonary hypertension with severe right heart failure.

The extreme usefulness of the disposable bag oxygenator in these two cases is impressive. Although acid citrate dextrose blood was obtained by the time of operation, it would not have been possible to obtain enough heparinized blood to permit the use of the disc oxygenator. The remarkable hemodynamic improvement in these patients in the immediate postoperative period is gratifying. As Cooley and Cross<sup>5</sup> have emphasized, the value of placing these patients on supportive partial bypass before the induction of general anesthesia seems indisputable. This seems to have facilitated the successful outcome of operation in the second case. Cannulation of the internal jugular vein is performed as easily as femoral vein cannulation and avoids postoperative problems related to groin phlebitis. Clamping the pulmonary trunk eliminates coronary return flow and the necessity of encircling the vena cavae. If a large catheter were placed in the internal jugular vein it might be possible to avoid caval cannulation via the right atrium. Thus attention could be directed to the pulmonary artery immediately after sternotomy.

The experience in the first case with postoperative hemothorax, requiring decortication on the 18th postoperative day, seems to support the advisability of inferior vena cava ligation as an adjunctive procedure. Thus, if it is necessary to discontinue anticoagulants during the postoperative period because of bleeding, the patient has the protection of caval ligation.

Angiograms with a centrally placed catheter

were not utilized in these cases but this is an essential step in the diagnosis of uncertain cases. Radio-active pulmonary scans<sup>18</sup> and determination of arterial-alveolar carbon dioxide gradients have been utilized in the diagnosis of pulmonary embolism but these measures do not seem necessary in cases of massive embolism.

## Summary

Two cases of massive pulmonary embolism occurring in postoperative patients have been presented. It is believed that emergency pulmonary embolectomy with the use of cardiopulmonary bypass prevented death in both cases.

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## Primary Amyloidosis With Death Due to Progressive Hypotension

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RENAL FAILURE without significant hypertension is known as a characteristic of amyloid renal disease. Yet severe, incapacitating hypotension, progressing to become a significant contributory cause of death, has been infrequently recognized as a complication of primary systemic amyloidosis. This report is of a patient in whom that occurred. A similar case was described previously by Schneckloth and Page.<sup>6</sup>

## Report of a Case

The patient, a 48-year-old Caucasian housewife, was put in hospital in April 1962, following sudden onset of colicky abdominal pain. The blood pressure was 110/60 mm of mercury and the pulse rate 100. Muscle guarding precluded adequate abdominal examination. Four plus proteinuria was noted. An x-ray film of the abdomen showed enlargement of the liver, with the lateral tip at the right iliac crest. There were two radiopaque densities to the right of the second lumbar interspace. An intravenous pyelogram showed equal bilateral excretion at five minutes. Partial obstruction at the right uretero-pelvic junction was seen.

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At operation a rough-surfaced, dark brown calculus 1 cm in diameter was removed. As the patient had persistent low-grade fever after operation, antibiotics were given. Motile Gram-negative bacteria and white blood cells were seen in a voided specimen of urine at the time of admission and in a catheter specimen taken at the time of retrograde pyelography.

The patient was discharged from the hospital but was readmitted two weeks later because of progressive weakness, dyspnea on exertion, orthopnea, palpitations and ankle edema. Despite the edema, she had lost about 20 pounds. Blood pressure was 90/64 mm of mercury, pulse rate 120 and respirations 36 per minute. The lungs were clear and the heart not enlarged. An x-ray film of the chest was within normal limits. An electrocardiogram showed sinus tachycardia, prolonged Q-T interval and ST-T wave abnormalities consistent with electrolyte imbalance. An intravenous pyelogram did not visualize the right collecting system. Right nephrectomy was done without complication. A tissue review and special stains made of the resected kidney showed extensive amyloid infiltration of the arterioles and glomeruli. In addition, there were foci of acute and chronic pyelonephritis. At home the patient did not improve. The albumin:globulin ratio was 1.5:2.1, serum cholesterol 424 mg per 100 ml and the protein content of 2,500 ml of urine, a 24-hour specimen, was 7.7 gm.

The patient was admitted to UCLA Hospital in July 1962. Two weeks previously she had noted some small intradermal purpura on the forearms. She reported loss of hair since the onset of illness. Examination showed chemosis of both eyes and resolving subconjunctival hemorrhage. The lymph nodes were not palpable. The lungs were clear, the heart not enlarged. Due to induration and tenderness from the previous surgical incision, the liver could not be adequately evaluated. The spleen was palpable 3 cm below the costal margin. One plus pitting edema was present to mid-tibia bilaterally. Rectal biopsy was negative for amyloid. After an eight-day course of sulfisoxazole the patient was discharged with prescription of a low salt diet, chlorothiazide and potassium chloride.

At home she had episodes of palpitation, lightheadedness, weakness, and sweating on limited ambulation. These symptoms were relieved by lying down. She was readmitted to UCLA Hos-

pital in September 1962. Blood pressure was 85/60 mm of mercury with the patient supine and fell to 70/50 mm when she sat up; at the same time the pulse rate increased from 84 to 132 per minute. The abdomen was protuberant and the flanks bulging. The liver and spleen were easily palpable about 2 to 3 cm below the costal margins. There was three plus pitting edema to the sacrum. She was given 50 gm of albumin intravenously and 100 mg of spironolactone by mouth daily for four days. The 24-hour urine protein after the first day of this therapy was 54 gm in 2,675 ml. Subsequently, the albumin:globulin ratio was 2.0:1.7. No abnormalities were seen on a radiographic series of the small bowel. Edema diminished considerably although some ascites remained. During the next month the patient was treated vigorously at home with hydrochlorothiazide, spironolactone and intermittent mercaptopurin injections. She lost about 4 kg in weight. On 19 November 1962 she fainted while waiting in the clinic. There was no detectable blood pressure and the pulse was weak and rapid. Intravenous infusion of 25 gm of albumin brought some improvement. On suspicion of adrenal insufficiency, prednisone was started in a dose of 10 mg daily. Diuretic therapy was discontinued for one week then resumed in reduced dosage after the reaccumulation of edema fluid. A trial of mephentermine initially caused a blood pressure response to 100/70 mm of mercury with the patient supine, but no blood pressure could be obtained on standing. As hypotension became worse when the effect of the drug was expended, it was discontinued.

In January 1963, the patient was readmitted and a 100 gm protein, low-sodium diet was begun and all drugs were discontinued. With this the 24-hour urine protein excretion varied from 24.4 to 28.5 gm. Bone marrow aspirate was moderately hypocellular; stainable iron was absent. Plasma cells made up 5.25 per cent of the total. The hemoglobin content of peripheral blood was 12.6 gm per 100 ml, the hematocrit 40 per cent. By measurement with radioactive chromium the red cell volume was 1,050 ml and the plasma volume 1,640 ml. On three successive days infusions of 300 ml of plasma were given. The patient gained about one pound a day and she began to have paroxysmal nocturnal dyspnea, orthopnea and anorexia. Thoracentesis was done on the left side and 960 ml of lactescent fluid with a specific gravity of 1.006 was withdrawn but there was

rapid reaccumulation. The only position in which she was comfortable was lying in bed at a 30° angle. She became faint when sitting up and dyspneic when lying flat. At this time the blood pressure was 55/40 mm of mercury supine and the pulse 110 per minute and regular. When measured in February, the blood urea nitrogen was 30 mg, creatinine 3.2 mg and albumin:globulin 0.5:2.4.

Again the patient was returned to her home but a month later, in March 1963, she had a cough productive of yellowish sputum, low grade fever and an increase in dyspnea, orthopnea, weakness and anorexia. She was readmitted to hospital. The blood pressure was 44/30 mm of mercury supine, the pulse rate 110 and respirations 28 per minute. Anasarca and wasting were striking. The liver was now 9 cm and the spleen 4 cm below the costal margins. The total serum protein was 2.6 gm per 100 ml with 12 per cent albumin (0.3 gm per 100 ml). The 24-hour urine volume was 260 ml, the serum creatinine 7.6 mg per 100 ml and carbon dioxide 15 millimols per liter. On admission 1,300 ml of clear yellow fluid was removed from the left pleural cavity. Fluid reaccumulated within 24 hours. She became stuporous and the blood pressure was unobtainable. Six hours later she died.

Throughout the course of illness there was a neutrophilic leukocytosis and the white blood cell count ranged from 10,000 to 24,000 per cu mm. The hematocrit never fell below 30 per cent. Platelets were reported adequate on all smears. Urinalysis showed specific gravity from 1.004 to 1.032, pH from 4 to 8, 3 to 4 plus protein, and no reaction for sugar or acetone. Urine sediments contained increased numbers of white cells and less often red cells, hyaline and granular casts and bacteria. On many occasions urine cultures grew more than 100,000 bacteria per ml of various species.

## Autopsy

At autopsy there were 1,700 ml of fluid in the left thoracic cavity and 900 ml on the right; the abdominal cavity contained 900 ml. Numerous pale, tan, firm lymph nodes 1 to 4 cm in diameter were seen throughout the mesentery and in the mediastinum. Gross evidence of amyloid was present in the spleen, which weighed 730 gm, and in the left kidney which weighed 200 gm. The renal vein was thin-walled and patent. The liver weighed

2,000 gm. Microscopic examination of the kidneys showed that all glomeruli contained large amyloid deposits. Foci of chronic pyelonephritis were scattered throughout the cortex. The spleen was almost entirely replaced by amyloid, while liver and lymph nodes contained a moderate amount and the adrenal glands, thyroid, tongue, heart and gastrointestinal tract were diffusely infiltrated with smaller amounts. Throughout most organs examined, including striated muscle, the walls of the arterioles and the intima of the arteries were composed of amyloid. The amyloid was characteristic, but it stained poorly with Congo red. Foci of acute purulent bronchiolitis were found. Comparison of microscopic sections of the right kidney, removed in June of 1962 with those of the left kidney, examined nine months later, showed an increase in the amount of amyloid in that time, especially in the glomeruli.

## Comment

The features of this case favor the diagnosis of primary amyloidosis. These include (1) the initial presentation of four plus proteinuria and enlargement of the liver, (2) the absence of a preceding history or of postmortem findings of a chronic illness known to be associated with the production of amyloidosis, (3) the finding of extensive infiltration with amyloid in the resected kidney two months after the onset of symptoms, (4) the poor staining of the amyloid with Congo red and, (5) the widespread involvement of smaller blood vessels.

The hypotension was attributed mainly to widespread amyloid infiltration of arterioles, hypovolemia and decreased venous return. Evidence of adrenal insufficiency was lacking. Responsiveness to corticotropin (ACTH) was normal when measured in July 1962. In January 1963, 24-hour urinary 17-hydroxy and ketosteroids were within normal limits (Table 1). Urinary sodium excre-

TABLE 1.—Results of Adrenal Function Tests\*

Date of Test	Steroid Contents (normal values in parentheses)		
	17-Keto steroids (6 to 15 mg)	17-Ketogenic steroids (5 to 8 mg)	17-Hydroxy- steroids (2.9 to 10.3 mg)
7-18-62 .....	7.9	17.2	.....
7-19-62† .....	9.7	38	.....
7-20-62† .....	18.2	62	.....
7-21-62† .....	20.1	63	.....
1-11-63 .....	6.4	.....	6.6

\*Expressed as milligrams of steroid per 24-hour urine collection.

†Following corticotropin stimulation.



tion was greatly diminished during the later stages of the disease (1 to 2 mg per 24 hours). At autopsy much of the adrenal cortex was preserved despite amyloid deposits. When clinical adrenal insufficiency occurs in association with amyloidosis, it is almost always the secondary form of the disease.<sup>3</sup>

Amyloid cardiomyopathy may have been a major contributing factor to the hypotension, although at no time during the course of the disease was enlargement of the heart demonstrated or murmurs heard.<sup>5</sup> On occasion cardiac amyloidosis may mimic constrictive pericarditis.<sup>1,4</sup> At autopsy the heart weighed 270 gm; the valves were flexible and without vegetation; the myocardium was substantially infiltrated with amyloid. Persistent tachycardia, even at rest, may indicate a response to hypovolemia and intact cardio-accelerator sympathetic nerves.<sup>7</sup> Hypovolemia was demonstrated by measurement of the radioactive chromium red cell blood volume at a time when no treatment was being given.<sup>8</sup> The role of amyloid infiltration of peripheral and autonomic nerves was not adequately assessed by tissue examination. Except for hypotension, symptoms and signs of neuropathy were not present.<sup>2</sup> Blood pressure response to mephenteramine was minimal and only in the supine position; no blood pressure could be obtained with the patient standing. This minimal blood pressure response in the absence of evidence of neuropathy suggests that amyloid infiltration of arterioles played a prominent role in bringing about hypotension.<sup>7</sup> The presence of rather pronounced muscle wasting and inactivity, causing impaired venous return, may have augmented the presumed low cardiac output.

Diuretic therapy was helpful in alleviating excess edema and pleural effusions, but vigorous diuretic therapy enhanced the hypotension and once caused the patient to faint. Elastic stockings on the lower extremities shifted the edema fluid to the chest and abdomen without affecting the hypotension. When infusions of albumin and plasma were given, a transient rise in blood pressure occurred. During the day or two following protein infusion, urinary protein excretion increased without much change in the serum proteins. Therefore these infusions were reserved for severe hypotensive episodes.

Uremia was mild until the terminal stage of illness, and it could probably be attributed as much to poor renal perfusion as to extensive

amyloid infiltration. The serum creatinine was probably a poor index of renal failure because of the muscle wasting, yet the creatinine-to-urea ratio was in the range expected.

## Summary

The clinical course and pathological findings are presented of a middle-aged woman with primary amyloidosis, nephrotic syndrome and progressive, incapacitating hypotension. The hypotension appeared to be due to widespread amyloid infiltration of arterioles, hypovolemia and decreased venous return to the heart, rather than to myocardial failure, autonomic or peripheral neuropathy or adrenal insufficiency. Uremia was attributed to poor renal perfusion in addition to amyloid deposits in the kidney. Infusions of plasma and albumin were of only transient benefit in raising the blood pressure and decreasing edema. Careful diuretic therapy was successful in controlling edema and pleural effusions, but excessive diuresis enhanced hypotension.

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### Generic and Trade Names of Drugs

Sulfisoxazole—Gantrisin®  
 Chlorothiazide—Diuril®  
 Hydrochlorothiazide—Esidrix®, HydroDiuril®, Oretic®  
 Spironolactone—Aldactone A®  
 Mercaptomerin—Thiomerin®  
 Prednisone—Deltasone®, Delta®, Meticorten®, Paracort®  
 Mephenteramine—Wyamine®

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# Thrombotic Thrombocytopenic Purpura and Systemic Lupus Erythematosus

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ALTHOUGH some investigators have noted an occasional association of thrombotic thrombocytopenia purpura (TTP) with systemic lupus erythematosus (SLE), the literature contains many reports denying the existence of any clinical or pathologic relationship between these entities. Levine and Stearn<sup>11</sup> reported both conditions present at the time of death in 23 per cent of a series of cases they reviewed.

In the case here reported, changes compatible with SLE from both the clinical and pathologic standpoints were found to be present with lesions of TTP occurring as a terminal episode.

## Report of a Case

A 39-year-old white housewife dated the onset of illness at age 17 when painful swelling of the left shoulder and right knee developed. At age 36 she had a recurrence involving fingers, wrists and ankles. Pleurisy on the left side also developed, and subsequently pleural effusion. A high dosage of salicylates was prescribed at that time. Two years later, at age 38, arthritis recurred shortly after a complete hysterectomy. Despite salicylates, the symptoms became more severe. Results of tests for rheumatoid arthritis and lupus erythematosus were negative. The erythrocyte sedimentation rate was increased. Use of salicylates was discontinued and chloroquine begun. The arthritic activity increased, with painful swellings of hands, wrists, left elbow and right knee. Pleurisy developed on the left side and an erythematous rash appeared on the malar areas. Three months later the patient was put in hospital because of an exacerbation of the joint and chest symptoms.

On physical examination the blood pressure was 180/90 mm of mercury, the pulse 90 per minute and regular, respirations 18 per minute and temperature 98.6°F. Crepitant rales were noted in the left lung base. A grade II to VI systolic murmur was heard at the apex and a grade II to VI diastolic murmur over the left

sternal border. The hemoglobin was 10.8 gm per 100 ml, the hematocrit 34 per cent. Leukocytes numbered 5200 per cu mm with a shift to the left of the neutrophils in the cell differential. Platelets were adequate. The reaction for albumin in the urine was three to four plus and on microscopic examination hematuria was noted. An electrocardiogram was interpreted as showing ventricular hypertrophy with eschemia and/or strain.

Prednisolone, 20 mg a day, and hydrodiuril, 50 mg a day, were given. The status of the patient remained unchanged for 72 hours except for a seven pound loss in weight and a decrease in chest pain. Blood urea nitrogen was 23 mg per 100 ml with an increase of serum creatinine to 1.8 mg per 100 ml. By the seventh hospital day, left pleural effusion developed. Two tests for lupus erythematosus were negative. Reaction to a direct Coombs test was weakly positive. Serum proteins were 7.6 gm per 100 ml, with albumin of 3.9 gm and globulin of 3.7 gm. A blood culture was negative and the antistreptolysin-O titer normal. When examined again on the fifteenth hospital day the urine was strongly reactive for albumin and there were 100 to 150 leukocytes and 50 to 60 erythrocytes per high power field. The blood urea nitrogen was 45 mg per 100 ml. Leukocytes numbered 16,300 per cu mm with a left shift. The patient was digitalized. On the nineteenth hospital day, serum potassium was 2.9 mEq per l and supplemental potassium therapy was begun. On the twenty-first hospital day, the patient complained of dyspnea, nausea and chest pain and there were episodes of vomiting and hemoptysis. A day later a generalized hemorrhagic rash suddenly appeared. At this time platelets numbered 46,000 per cu mm of blood, blood urea nitrogen was 102 mg per 100 ml and serum electrolytes were within normal range. The hemoglobin was 9.8 gm per 100 ml and the hematocrit was 33 per cent. Leukocytes numbered 15,000 per cu mm with a persistent left shift. On the twenty-third hospital day, the patient became mentally dull and was incontinent. Crepitant rales developed in the chest. Generalized convulsions occurred and calcium gluconate was given. By the twenty-fifth hospital day, the blood urea nitrogen was 114 mg per 100 ml, serum potassium 5.7 mEq and chlorides 91 mEq per liter. The patient's condition steadily deteriorated, urinary output decreasing, and she died on the twenty-sixth hospital day.

Submitted 15 October 1965.



## Pathologic Findings

On postmortem examination, fibrous adhesions were seen on serous surfaces of the body. There were fibrinous adhesions on the pericardium and petechiae on the epicardium. The heart weighed 525 grams with the left ventricular segment weighing 350 grams. Small granular and friable vegetations were seen on the ventricular aspects of two cusps of the aortic valve. On histologic examination of aortic valve an atypical verrucous lesion free of inflammation or bacteria was seen. Fibrinoid necrosis, fibrin thrombi and inflammation of vessel walls were present in the coronary arteries (Figure 1). Fibrinoid necrosis was seen in arterioles of splenic, hepatic and adrenal vessels, some with aneurysmal dilation. Fibrin thrombi were observed in these vessels, some of them appearing to be free within the lumen and some attached to the vessel walls. The kidneys together weighed 300 gm. The surfaces of the kidneys were hemorrhagic and on section there

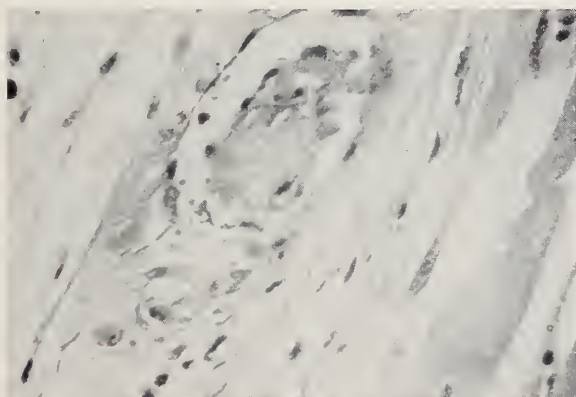


Figure 1.—Fibrin thrombus adherent to the wall of a small blood vessel in the myocardium. Hematoxylin and eosin stain,  $\times 450$ .

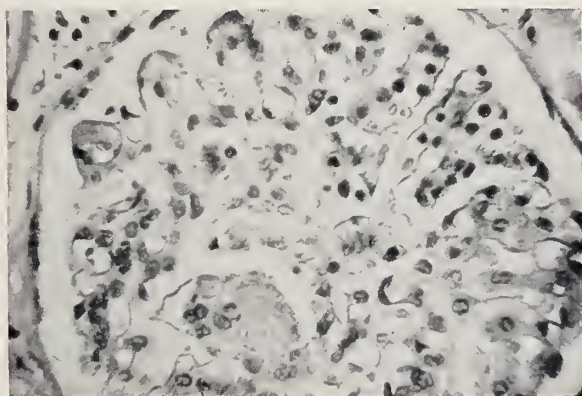


Figure 2.—Fibrinoid necrosis of arterioles of a glomerulus with basement membrane proliferation. Hyaline thrombi are present in the glomerulus. Hematoxylin and eosin stain,  $\times 1,000$ .

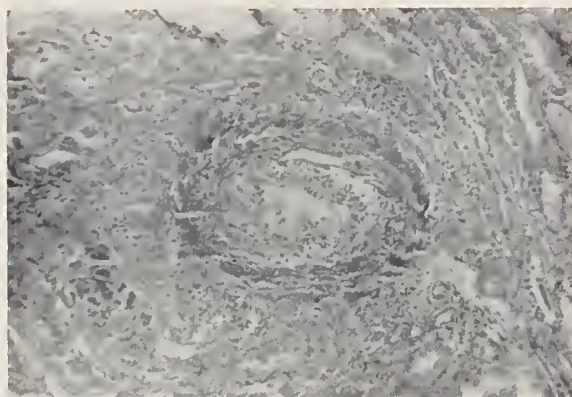


Figure 3.—Medium-sized renal artery involved in acute inflammation. Endothelial proliferation and necrosis is present. Hematoxylin and eosin stain,  $\times 125$ .

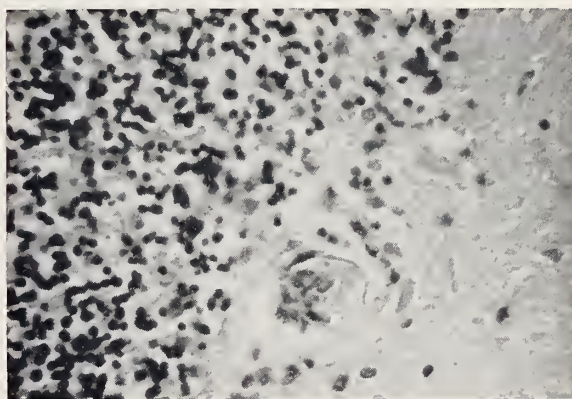


Figure 4.—Fibrin thrombi present in a cerebellar arteriole. Hematoxylin and eosin stain,  $\times 125$ .

were both old and new areas of infarction, with recent petechial and confluent hemorrhages as well. Microscopically, many of the glomeruli showed proliferation of the basement membrane with hyalinization resulting in "wire-loop" glomeruli in which fibrinoid necrosis had occurred (Figure 2). Hyaline thrombi were noted in the glomeruli. Both small and medium-sized arteries were involved (Figure 3). Petechiae were seen in the putamen, pons, medulla and cerebellum. There were fibrin thrombi in the meningeal, cerebral and cerebellar vessels (Figure 4). The bone marrow was hypercellular and megakaryocytes were increased. Fibrinoid necrosis and fibrin thrombi were present in the vessels of adipose tissue and skin. Histologic sections of skin revealed atrophy of the epidermis, with increase in collagen fibers, some areas of which had undergone fibrinoid necrosis.

## Comment

In this case the renal, splenic, endocardial and cardiovascular changes frequently associated with



systemic lupus erythematosus<sup>10</sup> were present, as were the manifestations of TTP, including intraluminal hyaline masses, endothelial proliferation and aneurysmal dilatation of small vessels.<sup>8,13,14</sup>

The thrombocytopenia found in TTP is a constant feature and is usually severe, resulting in petechial hemorrhages in the skin, mucous membranes and viscera.<sup>12</sup> Characteristically, this low platelet count is refractory to therapy. Hirsh and Gardner<sup>9</sup> reported that the survival time of transfused normal platelets in these patients is reduced. This observation, considered with the fact that bone marrow megakaryocytes were present in adequate number, leads to the conclusion that the thrombocytopenia is the result of peripheral platelet destruction. However, Craig and Gitlin,<sup>3</sup> using fluorescent techniques, were unable to demonstrate platelet components in these thrombi. They found that the thrombi consisted largely of fibrin. Using several tincturing methods, Fisher and Creed<sup>7</sup> concluded that the blood vessel change in TTP was fibrinoid degeneration which resulted in subendothelial accumulation of eosinophilic periodic acid Schiff-positive material. This substance is thought to be a precipitate of mucopolysaccharide with a protein,<sup>2</sup> the source of which is vascular endothelium.<sup>4</sup> It appears, then, that the primary lesion in TTP is vascular. The altered surface of vessels leads to the formation of thrombi that contain fibrin.<sup>8</sup> Partial occlusion of these small vessels results in traumatic destruction of both erythrocytes and platelets, leading to both the anemia and thrombocytopenia found in this disease.<sup>13</sup> The hemolytic anemia varies in its severity in TTP, and the direct Coombs test is almost invariably negative. However, in a few cases, such as the one here presented, the result of the test is positive.

This observation suggests that hemolysis is not caused by an antibody as in hemolytic anemia of the auto-immune type,<sup>5</sup> but possibly by an antibody present in the blood but not detected by the usual Coombs test reagent.<sup>6</sup>

Pathologic changes present in this case were consistent with SLE. The blood vessel alterations were not unlike those of that disease, although the larger blood vessel lesions noted in the present case are not as common in SLE. The vascular lesions present were those of the microangiopathic necrotides described by Dacie<sup>5</sup> and Alarcon-Segovia and Brown.<sup>1</sup>

The observations made by Levine and Stearn<sup>11</sup>

that the group of patients with TTP who manifest clinical evidence of SLE constitutes a subgroup within the total number of patients with TTP seem to apply in this case. If it is assumed that these patients have SLE, it may be safe to say that the immunologic and vascular alterations that take place in them may form an internal environment conducive to the development of TTP as a terminal event. This concept is supported by clinical and laboratory findings in the present case that were consistent with SLE followed by a fulminating terminal picture of TTP.

## Summary

A case report is presented of systemic lupus erythematosus with late manifestations of thrombotic thrombocytopenic purpura. A brief discussion of the etiologic factors of these disease entities is also presented.

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# Medical Staff Conference

## Acute Leukemia

*These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.*

DR. DONALD A. YOUNG:\* This is the third University of California Hospital admission for this 32-year-old man, a graduate student from Berkeley, who was admitted because of vomiting, weakness and malaise. The patient was in good health until May 1965 when he had onset of what he referred to as a cold with general malaise and fatigue. This continued and in June 1965, because of intermittent fever and cough, he sought medical attention at another hospital. A diagnosis of acute leukemia was made on examination of bone marrow aspirate and he was referred here for further evaluation. He was here from 16 June to 29 June 1965. Therapy was begun with prednisone and then with 6-mercaptopurine; and later, because of a positive reaction to a skin test for tuberculosis, isoniazid was added to the therapeutic regimen. The patient became febrile. *Salmonella montevideo* grew on cultures of stool and sputum. Sputum and gastric cultures were negative for acid-fast bacilli. He was treated with a large number of antibiotics during his stay in hospital. Three days after he was discharged he was readmitted because of recurrent fever, cough, diaphoresis and malaise. He was found to have pneumonia. During the second stay in hospital the number of leukocytes decreased from 83,000 per cu mm of blood to 900. Platelet count, however, remained normal and the bone marrow continued to show leukemic cells. Discharged after a month in hospital, he was readmitted not quite three weeks later because of persistent nausea, vomiting, cough, fatigue, malaise and a very low hematocrit.

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On physical examination he seemed to be in no acute distress. There were no petechiae noted in the skin but there were flame hemorrhages in the fundi of both eyes. There were no palpable lymph nodes. Dullness was noted at the base of the right lung and fremitus and breath sounds were decreased. The liver and spleen were not enlarged.

Laboratory data at the time of this admission: Leukocytes, 600 per cu mm; packed red cell volume, 17 per cent; hemoglobin, 9.7 per 100 ml; platelet count (as in preceding two months) remained in the 100,000-250,000 range, and cultures again showed *Salmonella montevideo* in sputum and stool. Numerous blood and urine cultures were negative for pathogenic organisms.

DR. LLOYD H. SMITH, JR.:† This patient was referred to us by Dr. Gilbert Roberts.

DR. GILBERT ROBERTS: When he was admitted to the hospital, he had a mediastinal mass, right pleural effusion, and enlargement of cervical lymph nodes on the right side. Our diagnosis was Hodgkin's disease, not leukemia. Biopsy was done and the diagnosis was established by marrow aspiration.

Dr. Smith: I believe there are x-rays to be seen.

### Roentgenographic Features

DR. WARREN RUSSELL‡: The x-ray films present a rather interesting chronology of the patient's course. The first film of the chest, taken 17 June, shows a very pronounced widening of the mediastinum and a rather faint infiltrate extending out to

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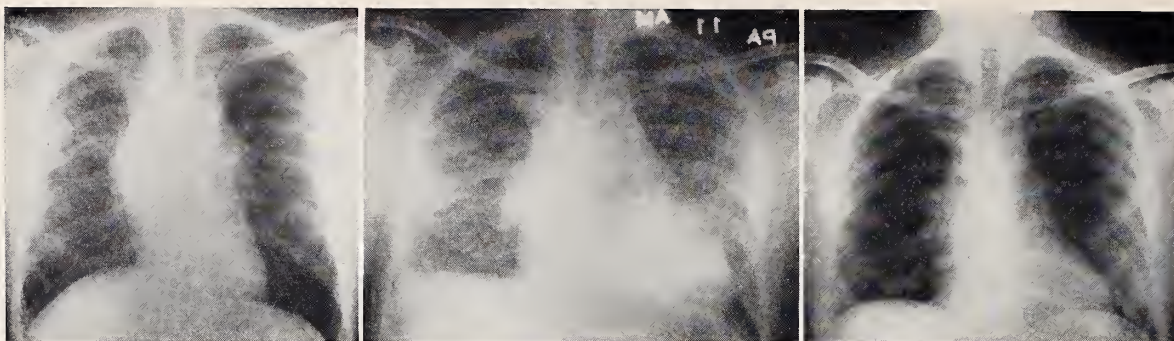


Figure 1.—Film at left, taken 17 June, shows pronounced widening of the mediastinum and faint infiltrate extending out to lung fields. Center film, 23 July, shows progression to bilateral pulmonary infiltrates. A film taken 3 September (right frame) shows considerable regression of radiographic abnormalities—the lung fields essentially clear and the mediastinum not as wide as it had been for two and a half months earlier.

the lung fields. By July this had progressed to bilateral pulmonary infiltrates. The most recent film, 3 September, shows decided regression of the radiographic abnormalities, with lung fields essentially clear and the mediastinum, although still wide, much less so than at first (See Figure 1).

*Dr. Smith:* Thank you, Dr. Russell. The patient is not being presented this morning because of the degree of his illness. The discussion will be led by Dr. Bruce Lewis§ and Dr. Martin Cline.¶

### Clinical Manifestations

DR. BRUCE F. LEWIS: Acute leukemia—"suppuration of the blood," as it was called by Bennett in 1845—comes to clinical notice in a variety of ways. The patient that Dr. Young presented is a rather typical example of adults with acute myeloblastic leukemia. As is the rule in this disease, the patient has not responded to therapy. He has had a variety of complications mostly of an infectious nature, and it appears that the disease is progressing inexorably.

We could have presented a different patient this morning—for example, a woman 23 years of age, whom we have observed periodically over the last nine months or so. Newly married, she came to the hospital for the first time shortly after her honeymoon because of persistent fever, weakness and a high leukocyte count. As it turned out, she had acute lymphoblastic leukemia. After treatment with corticosteroids, she had a very rapid remission of disease; and on a program of alternating 6-mercaptopurine and methotrexate, it has been in remission ever since. In the course of the disease central nervous system leukemia (which I shall discuss later) developed. This condition

which we have come to consider an expected feature of lymphoblastic leukemia, was successfully treated and the patient is continuing to do well. Thus, there are basically two types of acute leukemia: on the one hand, acute myeloblastic and monoblastic leukemia, which are clinically very similar; and on the other hand, acute lymphoblastic leukemia. In contrast to acute myeloblastic leukemia, acute lymphoblastic leukemia usually responds to therapy, at least initially, and has a somewhat more benign course. Since treatment for the two diseases is different, it is important to make an accurate morphological diagnosis.

There are other clinical syndromes that are seen in leukemia. For example, a number of older persons have been described who have anemia, chronic unexplained leukopenia, or thrombocytopenia. Eventually after a period which may run for several years, the typical features of acute myelogenous leukemia develop and the typical course of that disease ensues.

Acute lymphocytic leukemia is somewhat more common than the combination of acute myelocytic and acute monocytic leukemia. In all forms of acute leukemia male patients outnumber females about three to two. Most of the patients with acute lymphocytic leukemia are of the pediatric age group, and there is a sharp peak in the incidence of acute lymphocytic leukemia at about the age of three. After that age, the incidence of lymphocytic leukemia falls off sharply. As the incidence of granulocytic and monocytic leukemia does not change appreciably during life, these forms of acute leukemia are the most common in the elderly.

The signs and symptoms of leukemia can be related to just a few factors: leukemic proliferation of the marrow, leukemic infiltration of other or-

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gans and poorly understood metabolic alterations. As a result of leukemic proliferation in the marrow, deficiencies develop in production of red cells, white cells and platelets, leading to the familiar problems of anemia, bleeding and infections. Leukemic infiltration of other organs result in hepatosplenomegaly or lymphadenopathy or both. Since any organ can be infiltrated by leukemia, a variety of symptoms may result. Metabolic alterations may cause symptoms such as weakness, lassitude or fever which cannot be adequately explained.

Physical findings in acute leukemia can also be related to these same factors. An important finding is sternal tenderness, which can be present in as many as two-thirds of patients with acute leukemia. It has been pointed out that patients who have sternal tenderness tend to do somewhat less well than patients who have not. Lymphadenopathy and hepatosplenomegaly are common, being somewhat more common in the lymphoblastic form of leukemia than in the myeloblastic or monocytic forms. Skin infections are particularly common in myeloblastic leukemia, and infiltration of the gums is common in monoblastic leukemia. However, in all forms of leukemia a variety of skin manifestations can be present, frequently due to leukemic infiltration of the skin. Hemorrhagic phenomena of all sorts occur with leukemia, including petechiae, purpura and ecchymoses. There may be evidence of bleeding from any site.

So far as diagnosis of acute leukemia is concerned, this is almost exclusively morphologic at the moment. It is a diagnosis which is usually considerably simpler for the hematologist studying the living patient than for the pathologist at autopsy. The reasons for this are multiple. Very few patients with acute leukemia die without having had treatment, and treatment may erase all the manifestations including marrow and organ infiltration. In addition, recently there have been reports of patients with typical acute leukemia who died without receiving cytotoxic therapy, and who had no evidence of organ and marrow infiltration at autopsy. In life, the diagnosis can usually be made from the peripheral blood. About 60 per cent of patients with acute leukemia have high leukocyte counts. Forty per cent have low or normal counts. In some cases, no abnormal cells will be found in the peripheral blood; then the diagnosis can be made only by examination of the bone marrow. Classically, the bone marrow in acute leukemia is

densely infiltrated with immature leukemic cells. A variety of clues may enable differentiation between lymphoblastic and myeloblastic leukemia. The presence of granules in developing cells, particularly peroxidase-positive granules, indicates a diagnosis of either myeloblastic or monoblastic leukemia. Auer rods which are eosinophilic cytoplasmic rods can be found in as many as 50 per cent of patients with myeloblastic leukemia and are probably pathognomonic for either myeloblastic or monoblastic leukemia.

**D**IFFERENTIAL diagnosis in acute leukemia involves a number of different hematologic syndromes such as aplastic anemia, agranulocytosis, idiopathic thrombocytopenic purpura and infectious mononucleosis. If the bone marrow is examined, however, there should be little confusion in making the diagnosis of acute leukemia. The only disease which presents much of a problem in the differential diagnosis is neuroblastoma, and it is confined largely to the pediatric age groups. A word should be said about leukemoid reactions and particularly the coincidence of tuberculosis and acute leukemia. There is no evidence that the incidence of leukemia is higher in patients with tuberculosis than it is in the general population. Nonetheless, the two diseases are frequently associated, and in occasional cases one may wonder whether tuberculosis is causing an atypical leukemoid reaction resembling acute leukemia. Unfortunately, there is no really good evidence that this has ever taken place, although the literature contains many suggestive cases.

I would like to discuss some of the common clinical problems that arise during the course of acute leukemia. The first is the occurrence of fever. This can be a very perplexing problem because sometimes, as exemplified by the patient presented this morning, extensive investigations yield no explanation for the fever. Fever occurring early in the course of acute leukemia is usually due to the disease itself and not to infection. However, as the disease progresses, fever is increasingly likely to be due to infection; and very unusual pathogens may be involved. It is important to do multiple cultures. A negative result of examination of the urine does not rule out the presence of a urinary tract infection, since the cellular response to infection can be so deficient in leukemic patients.

The second complication, hypercalcemia, is not at all as common as fever but I am mentioning it

merely to call it to your attention. Hypercalcemia is not nearly as frequent in acute leukemia as it is for example in multiple myeloma, but it has been reported with increasing frequency in recent years and we ourselves have seen one case in the last year.

Complications from abnormalities of uric acid metabolism are very frequent in patients with acute leukemia. Prodigious levels of serum uric acid may develop, resulting in deposition of urate in the tubules and in uric acid blockade of the kidney. This event can occur in at least two circumstances: shortly after the initiation of therapy, and when the leukocyte count is rising rapidly. The uric acid complications can usually be handled reasonably simply, first by the administration of large amounts of fluids, and second by keeping the urine alkaline. To this end we routinely give patients with acute leukemia sodium bicarbonate during the day and a small dose of acetazolamide (Diamox®) at night. We determine the urinary pH at least four times a day and try to maintain it between six and seven. Four-hydroxypyrazolo-(3,4-d) pyrimidine (Allopurinol®) may also be useful in difficult cases.

**H**YPOFIBRINOGENEMIA has been thought by some to be characteristic of acute promyelocytic leukemia, a variety of leukemia in which the predominant cell in the marrow is the promyelocyte rather than the blast. However, it is not possible clinically to differentiate between promyelocytic and myelocytic leukemia on any other basis; and, indeed, hypofibrinogenemia has been reported in many cases of acute myeloblastic leukemia. The cause of the hypofibrinogenemia is usually unclear. In some patients fibrinolysis has been demonstrated; in others, intravascular coagulation. In at least one reported case of acute myeloblastic leukemia, intravascular coagulation was successfully treated for a short period with heparinization.

The final problem for discussion is central nervous system leukemia. This develops, as I mentioned earlier, almost as a rule in patients who are successfully treated for acute leukemia, more frequently in acute lymphoblastic than in myeloblastic leukemia. The drugs that are commonly used for maintenance therapy, namely, methotrexate and 6-mercaptopurine, do not cross the blood-brain barrier to any extent. Consequently, the central nervous system can be a relatively immune reservoir for the development of leukemic cells.

Frequently, the symptoms of this complication are minimal. The most commonly reported symptom is headache, and unless the physician who is attending the patient is aware that it may stem from leukemic involvement of the central nervous system, he may attribute it to tension or sinusitis, or perhaps ignore it. Nausea and vomiting are the second most common symptoms. Involvement of the cranial nerves may occur, usually either the seventh or sixth cranial nerves. The point to bear in mind is that if a patient with acute leukemia has a persistent headache for a few days which cannot satisfactorily be explained, lumbar puncture is mandatory and will usually reveal an increase in pressure. In addition, increased protein is frequently seen, as well as an increased number of cells, which may be leukemic. Decreased sugar content is a somewhat less common feature. Patients who have central nervous system leukemia can be treated in a variety of ways, such as by x-ray therapy to the brain or by lumbar puncture alone. We have recently been treating all of our patients with central nervous system leukemia by intrathecal injection of methotrexate and have had excellent results. This brings us to a discussion of therapy in this disease.

The first type of therapy is supportive. Blood transfusions are used to correct anemia. Platelet transfusions can be of great help although in adults it is very difficult actually to raise levels of circulating platelets. Infections in children have been treated by transfusions of granulocytes, but this has not been a practical procedure for wide use, since it is so difficult to obtain adequate numbers of granulocytes. The drugs in common use are adrenal steroids: vincristin, which acts by mechanisms which are so far unexplained, methotrexate, a folic acid antagonist, 6-mercaptopurine, an anti-purine, and cyclophosphamide, an alkylating agent. Prednisone and vincristin, given separately, are the most effective drugs in producing a remission in children with acute lymphoblastic leukemia. They are almost as effective in acute lymphoblastic leukemia of adults. In acute myeloblastic leukemia, none of the drugs is very effective. Six-mercaptopurine appears to be the best of the drugs but even with this drug the remission rate is only about 15 per cent. There has been a good deal of discussion recently about the possibility that adrenal steroids might be contraindicated in patients with acute myeloblastic leukemia. The evidence for this is not compelling. In some instances steroids may be of



benefit. The combined use of drugs has been shown to bring remission in a higher proportion of cases. For example, in acute lymphoblastic leukemia of children the simultaneous use of prednisone and vincristin has given approximately an 80 per cent remission rate. In addition, it has been shown that maintenance therapy will lengthen a remission once it is achieved. The drugs that have been most effective in this regard are methotrexate and 6-mercaptopurine. The toxicity of these drugs is well known. As far as prednisone is concerned, it is of some interest that bleeding ulcers have been reported in patients with acute leukemia who are being treated with this drug, but this is not a frequent complication. Vincristin commonly causes peripheral neuropathy. Methotrexate may cause mucous membrane ulcers and marrow depression, while 6-mercaptopurine causes gastrointestinal distress and marrow depression. Of all these drugs, 6-mercaptopurine is most likely to cause jaundice, usually due to cholestatic hepatitis. Cyclophosphamide is a marrow depressant.

There are a variety of experimental programs which are being considered at the moment, including the simultaneous use of several of these drugs in very large oral or intravenous doses. It has been possible, using such a regimen, to obtain remission in as high as 40 per cent of patients with acute myeloblastic leukemia. Whether this will be of any practical utility remains to be shown.

The final question is: Does all this therapy really help the patient with acute leukemia? Are we doing anything beneficial when we treat patients with acute leukemia? I think you would agree that we probably are. The data of Freireich and Frei which was recorded in the *Journal of Chronic Disease* some years ago demonstrate the improvement in survival in patients with acute lymphocytic or myelocytic leukemia who have remissions. If a patient has a remission, his survival is prolonged over that of the patient who does not have a remission by about the duration of remission. This prolongation is not a very substantial one in most cases, however, and the course is almost inevitably tragic. One can only hope that some of the work that Dr. Cline is going to tell us about now will lead to more successful therapy of acute leukemia.

### **Etiologic Considerations**

DR. MARTIN J. CLINE: The concept that a mutation in a hemopoietic cell line is responsible for

leukemia has been with us for about a quarter of a century. By mutation, I mean an acquired abnormality of genetic material as opposed to one that is inherited. As the discussion unfolds, you will see that the distinction between an acquired and an inherited abnormality may be a rather fuzzy one. What is the basis of this mutation theory? At first it was based on the observation that there was very little evidence for an inherited tendency in human leukemia. Subsequently it was shown that, in animals exposed to known mutagenic agents, there was an increased incidence of leukemia. Most conclusively, it has been shown recently that in virtually every case of human acute leukemia there are abnormalities of the chromosome patterns of the leukemic cells which are not found in the hemopoietic cells of near relatives. These chromosomal abnormalities are either aneuploidy, polyploidy or structurally abnormal chromosomes.

If leukemia is a mutation, the questions that can logically be asked are: What are the known mutagenic agents and what is the evidence implicating each of these in acute leukemia? The known mutagenic agents can be simply summarized. These are ionizing irradiation, chemical mutagens and viruses. I would like to examine the evidence implicating each of these in acute leukemia.

Let us first examine radiation leukemogenesis. It is well known that ionizing irradiation can induce alterations in deoxyribonucleic acid (DNA). It can produce breaks in the DNA chain or cross-linking of the twin strands of the DNA molecule. In bacterial systems, ionizing irradiation increases the incidence of mutation; irradiation can produce murine leukemia.

Most pertinent to this discussion perhaps is the epidemiologic evidence implicating radiation in leukemogenesis in man. The great bulk of the evidence in this area has been accumulated from the studies of the survivors of the bombing in Hiroshima. Important information has been gained from these studies. First of all, above a dose of approximately 80 rads, there appears to be a linear increase in the incidence of leukemia with an increase in the dose of radiation. A person who was standing approximately a thousand meters from ground zero at the time of the detonation subsequently had a 30-fold increase in the likelihood that leukemia would develop. The closer he approached the hypocenter, the greater were the chances that leukemia would develop.

The second important point that emerged from these studies was the observation that there is a latent period between exposure to ionizing radiation and the development of leukemia. This period varied between two and 15 years but the greatest incidence was at about six years, or in 1951. Another fact that emerged was that the morphologic type of leukemia that subsequently developed appeared to be related to the age of the victim at the time of exposure: In children, lymphoblastic leukemia developed; in adults, myeloblastic leukemia.

The evidence obtained from the other studies all tends to support the evidence acquired from the studies in Hiroshima. These include: leukemia in children previously exposed to thymic irradiation, leukemia in patients treated with Iodine<sup>131</sup> for hyperthyroidism or by radiation of the spine for ankylosing spondylitis, the more controversial studies of increased incidence of leukemia in children after exposure to intrauterine irradiation, and the increased incidence of leukemia in radiologists. There are more than 300 well-documented reported cases of leukemia associated with excessive exposure to ionizing radiation.

ONE MAY LOGICALLY ASK whether radiation works directly or by way of an intermediate. It is known in bacterial systems at least that radiation can activate lysogenic viruses—that is, bacteriophage which is present in the bacterial cell but which is essentially dormant. The viral genetic information is present but it is not expressed until it is activated by ionizing radiation. At that time, the bacteriophage replicate and destroy the host cell. There is at least one analogy for this situation in mammalian systems. In certain strains of mice in which leukemia is induced by ionizing irradiation, the leukemia may be subsequently transmitted by a cell-free filtrate, or presumably by a virus. It should be noted that in bacterial systems at least the genetic information of the lysogenic virus may be transmitted along with the host cells' DNA; thus the distinction between an inherited and an acquired anomaly may be difficult.

The evidence for chemical leukemogenesis is less secure. Chemically induced alterations in DNA are known and certain agents are capable of producing mutations in bacterial systems. It is known that methylcholanthrene can produce leukemia in certain strains of mice, but the epidemiologic evidence implicating chemicals in acquired leukemia

in man is not so strong. Such evidence as exists is based largely on the observation that in many persons who have had long exposure to benzene, first aplastic anemia will develop and then, after a latent period of years, leukemia. Reports of this phenomenon have been largely from the Italian literature.

Since the observation by Gross in 1951 that a mouse leukemia could be transmitted by a cell-free filtrate, the viral theory of leukemogenesis has been increasingly exercised. Supporting evidence for such a theory can be divided into five categories: (1) the analogy with virus-associated animal leukemia, (2) the sporadic outbreaks of human leukemia, (3) the rather interesting evidence obtained in Burkitt's lymphoma, (4) the reported observation of virus-like particles in the blood of leukemic patients and (5) the rather controversial reports of isolation of these viruses. I should like to discuss each of these categories.

First of all, the mouse leukemias. In 1941, Cole and Furth described a mouse strain with a high incidence of spontaneous leukemia. As I have noted, a decade later Gross showed that this leukemia was due to a virus. Among the important facts that have subsequently emerged from the study of these leukemias are the following observations: After inoculation of the susceptible mouse with a virus, there is a latent period of months before the development of leukemia. During this period it can be shown that the thymus gland is the principal and primary site of proliferation of the virus. It is interesting that thymectomy also decreases the incidence of leukemia induced in certain mice by chemicals and by exposure to radiation, suggesting that a virus may be involved in these situations as well. It has been shown that the isolated nucleic acids of these viruses alone can increase the incidence of leukemia in susceptible mice. The story for avian leukemia is in essence quite similar to that for the rodent leukemia, and I won't discuss these in any detail. But I will note that as early as 1908 it was suggested that there might be an association of a virus with avian leukemia.

Sporadic outbreaks of human leukemia have been reported since 1923. The most recent and best studied of these occurred in a small parish in Niles, Illinois. Eight cases were involved. The most important observation implicating a transmissible agent such as a virus was the finding of antibodies to leukemic antigens in the parents and



siblings of patients. Such antibodies were not found in a control population.

Burkitt's lymphoma is an exceedingly interesting disease entity which may be related to the problem of viral leukemogenesis and tumorigenesis. It is a lymphoma with characteristic clinical and pathological features and it may occasionally involve the circulating blood. One of its most interesting features is its geographical distribution. It is found almost exclusively in a band across the tropical area of Africa, from Kenya and Tanganyika in the east to Dakar in the west. It is found in altitudes variously reported as 3,000 to 5,000 feet. In Africa, it accounts for some 50 to 70 per cent of all malignant disease in children. But it is not a disease of African children alone. It is a disease of children in Africa; that is to say, Europeans, Berbers and other racial groups living in this area are also affected by the disease. On the basis of its distribution in a hot, moist, tropical area and at low altitudes it has been suggested that an arthropod vector may be involved, and recently there have been claims for the isolation of a filtrable agent from the serum of patients with this lymphoma.

It is quite clear that in the blood of some patients with acute leukemia there are particles which resemble those which have been described in the rodent leukemias. In their initial studies Dalton and his colleagues at the National Institutes of Health found such particles in some seven of 50 patients. Kresley at Oakridge found them in the majority of leukemic patients.

The questions that could logically be asked at this point are: Are these particles viruses? And if they are viruses, are they etiologically related to leukemia? The question of whether they are viruses cannot be answered definitely at present. As to their etiologic relationship to leukemia, there are two schools of thought. One, which we might call the predestination school, believes the leukemic cell is going to become leukemic anyway and happens to be a good culture medium for passing viruses. The activist school believes that these viruses are leukemogenic. Neither group has incontrovertible evidence.

Can these agents be cultured? There are many reports of failures and few of successes. The early reports of successes have now been opened to question since the demonstration that the agents involved were in fact not viruses but were myco-

plasma; that is, agents like the Eaton agent that cause primary atypical pneumonia. These are the smallest of free-living organisms. They are somewhere in the evolutionary chain between viruses and bacteria and have many of the characteristics of viruses. Whether they are etiologic in leukemia is moot. At least we know that they do cause one human disease.

There is one other bit of evidence that viruses may be leukemogenic in man—evidence that is acceptable at least to virologists. Material isolated from patients with lymphoblastic leukemia and from Burkitt's lymphoma can interfere with the proliferation of other viruses in tissue culture.

If viruses are leukemogenic, how do they induce mutation and how do they alter cell metabolism? Well, the tumorigenic viruses in mammals as opposed to leukemogenic viruses are all DNA viruses, sv 40, polyoma, and some of the adeno viruses. These can induce chromosomal breaks similar to those I have shown. They have the interesting characteristic that after infection they appear to disappear from the cell. Their antigens can be found and the malignant transformation persists but the viruses are no longer present. In contrast, in avian and murine leukemia, the viruses involved are ribonucleic acid (RNA) viruses. These viruses stay around and can infect new host cells. The alterations in the cell's economy which can be induced by such viruses can be briefly summarized. The DNA and RNA viruses essentially act by interfering with transcription of the host DNA, so that the host messenger, RNA, is no longer formed. Instead, viral messenger RNA is made, and viral proteins are made, including the enzymes necessary for the synthesis of specific viral genetic material. In essence, then, the virus subverts the cell's economy for its own purposes.

What are the prospects in therapy if viruses are etiologic in leukemia? First of all, one may consider attempting to interfere with cell infection either with interferon, by specific vaccination, by chemical means or by viral means. Included in our list of references is a paper<sup>1</sup> that describes the use of viral agents to treat acute leukemia. However, if the viruses involved are DNA viruses and disappear from the cell after inducing leukemia, then suppressing infection is a little like locking the barn after the horse is gone. It may be more rational therefore to attempt to interfere selectively with the acquired biochemical aberrations of the leukemic cell, and this to some extent is the

rationale of present day chemotherapy. And lastly, there is the concept of introduction of new genetic material. This is quite feasible in vitro. It has been shown that if one isolates liver RNA and adds it to a culture of Hela cells, the Hela cells will then make albumin like the liver. There has already been one trial of the use of normal RNA instilled in the sternal marrow of a leukemic patient with the claim that there was a subsequent normal differentiation of the leukemic cells.

In summary, the evidence is exciting and intriguing, but by no means conclusive, that viruses are leukemogenic in man. The principal problems to be resolved are the isolation of specific viral agents which can be shown to be cytopathic for mammalian tissue culture material, and then the induction of leukemia by such agents in experimental animals. We have a long way to go before we fulfill Koch's postulates.

EDITOR'S NOTE: Shortly after presentation of this case, the patient was treated with a combination of prednisone, 6-mercaptopurine, vincristin and methotrexate. A complete hematological remission ensued. At present, six months later, the patient is on a regimen in which 6-mercaptopurine is alternated every four to six weeks with methotrexate. He is in complete remission.

#### ACUTE LEUKEMIA

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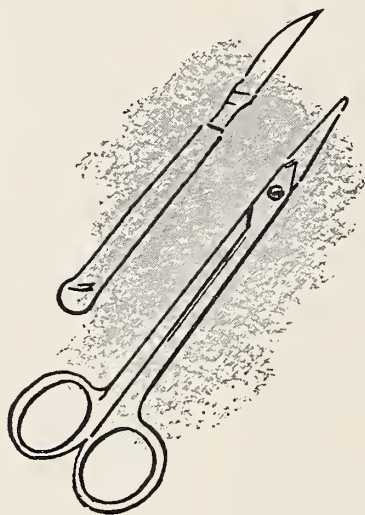
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## EDITORIAL

### An Important Meeting in Prospect

THE CALIFORNIA MEDICAL ASSOCIATION at its annual meeting later this month will serve in two ways—one scientific, the other political—its continuing purpose of developing the best possible medical care and supplying it with the least possible encumbrance.

On the scientific side, this year's program appears to be one that will add to a growing momentum of quality for which the Committee on Scientific Assemblies and the various Scientific Sections are to be congratulated.

Politically, one outstanding problem among the many items of policy that will confront the House of Delegates, is the matter of finding the best ways to supply medical care to the aged and needy under recently enacted federal and state programs. To the end that the quality of care shall not deteriorate as it has in other nations of the world where the state has come between physicians and patients, the medical profession must maintain a strong line of influence in designing and monitoring the machinery by which the government plans are to be carried out. The deliberations and the actions taken by our House of Delegates to make these plans reasonably work-

able will of course be given studious attention not only by other medical associations but by interested governmental agencies as well.

Quite understandably in light of the rising quality of our scientific sessions in recent years, this component of the California Medical Association's burgeoning program of continuing medical education is attracting more and more attention from practicing physicians and educators the country over. Each year the Committee on Scientific Assemblies receives inquiries in increasing numbers from physicians in other parts of the land who contemplate attending our meetings.

On perusal of the program (see February issue of CALIFORNIA MEDICINE) it becomes quite obvious why we attract the attention of alert physicians who are interested in keeping informed of the newest and most practical developments in the field of medicine. Considering what we have to offer—an excellent program given at a time of year when climatic differences are a further inducement for physicians from other parts of the country—one need not be a gifted seer to predict that sooner or later the CMA will begin to advertise its scientific sessions well beyond the borders of our state and perhaps charge a moderate registration fee for out-of-state registrants.

Whatever the future of either our scientific meetings or the necessary concern of medical organizations with governmental machinery involved in the supplying of physicians' services to certain of our citizens, we can look forward to our meeting 19 to 23 March in Los Angeles as an important one.

# California Medical Association



## NOTICES AND REPORTS

### Council Meeting Minutes

*Tentative Draft: Minutes of the 517th Meeting of the Council, Airport-Marina Hotel, Los Angeles, January 16, 1966.*

The meeting was called to order by Chairman Anderson in the Airport-Marina Hotel, Los Angeles, Sunday, January 16, 1966, at 9:30 a.m.

#### Roll Call

Present were President Teall, President-Elect MacLaggan, Speaker Quinn, Vice-Speaker Telford, Editor Dwight L. Wilbur, Secretary Hosmer and Councilors Isenhour, Wilson, Melone, Todd, Gooel, Bullock, O'Connor, Rogers, Maguire, Burnett, Richard S. Wilbur, Miller, Watts, Fenton, Kay, Kaiser, Taw, Ham, Anderson, Yant, Grunigen and Shaw. Absent for cause was Immediate Past President Doyle.

A quorum present and acting.

Present by invitation were Messrs. Clancy, Collins, Klutch, Eberlein, Thomas, Goldman, Whelan, Blackley, Bowman, Clark, Moreillon, Garrick, Doctor Miller, Miss Price, Mrs. Redfern and Mrs. Griffith of CMA staff; Messrs. Hassard and Huber, legal counsel; component society executives Scheuber of Alameda-Contra Costa, Rideout of Butte-Glenn, Geisert of Kern, Lingerfelt of Fresno, Baker of Los Angeles, Bannister of Orange, Walters of Riverside, Donmyer of San Bernardino, Nute of San Diego, Neick of San Francisco, Thompson of San Joaquin, Wood of San Mateo,

Marvin of Santa Barbara, Donovan of Santa Clara, Brown of Sonoma, Collins of Marin, Doctor Lester Breslow, director of the Department of Public Health; Mrs. Jeanette Gentile, president of the California Medical Assistants Association; Doctor William Thompson and Messrs. Paolini, Wahlberg, Heller, Babb, Lemming and Bentley of California Physicians' Service; Messrs. Read, Salisbury and Brown of the Public Health League; Mr. Jerry Gould of the AMA; Messrs. Jackson and Cumming of the California Hospital Association; Doctors Bostick, Peck, Herzog, George Andersen, Halter, Boyers, Cobb, Kilroy and others.

#### Audio-Digest Foundation

The Council recessed to permit the annual meeting of the administrative members of Audio-Digest Foundation, Doctor Carl Anderson presiding.

Editor Claron Oakley reported on the editorial progress of the organization, noting that in the past 12 years over \$250,000 has been contributed to medical education. Audio-Digest is experiencing a 10 per cent annual rate of growth and is now expanding rapidly in international exchanges.

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RALPH C. TEALL, M.D. . . . .	President
JAMES C. MacLAGGAN, M.D. . . . .	President-Elect
WILLIAM F. QUINN, M.D. . . . .	Speaker
JOSEPH W. TELFORD, M.D. . . . .	Vice-Speaker
CARL E. ANDERSON, M.D. . . . .	Chairman of the Council
ALBERT G. MILLER, M.D. . . . .	Vice-Chairman of the Council
MATTHEW N. HOSMER, M.D. . . . .	Secretary
DWIGHT L. WILBUR, M.D. . . . .	Editor
HOWARD HASSARD . . . . .	Executive Director

General Office, 693 Sutter Street, San Francisco 94102 • 776-9400  
 ED CLANCY . . . . . Southern California Office  
 1515 N. Vermont Avenue, Los Angeles 90027 • 663-8071



Business Manager K. L. Hamman announced that he expected Audio-Digest could contribute another \$50,000 this spring to medical education. Since the inception of the organization, subscriber physicians have paid over \$5 million for its services, according to Mr. Hamman.

The administrative members present complimented both Mr. Oakley and Mr. Hamman for the excellent work done during the past year.

Doctor James C. MacLaggan, chairman of the CMA Committee on Committees, offered a list of nominees for the Audio-Digest Board of Directors. These were: Doctors Gordon Beckner, W. D. Evans, Elmer F. Gooel, George C. Griffith, Merlin A. Hendrickson, Donald D. Lum, Robert L. Marsh, John W. Pender, Edward B. Shaw, Donald Shelby and Keith P. Russell, and Messrs. Claron Oakley and K. L. Hamman. (The President and President-Elect are ex-officio members.)

**ACTION:** *Voted to accept unanimously the list of nominees submitted.*

The Council then reconvened to conduct the business of this 517th Meeting, a quorum present and acting.

#### 1. *Recognition of Dr. Arthur Kirchner*

Chairman Anderson announced the death of Dr. Arthur Kirchner (on January 3, 1966), holder of many offices at all levels of organized medicine.

**ACTION:** *Voted to adjourn the 517th meeting of the CMA Council in honor of Doctor Kirchner.*

#### 2. *Minutes for Approval*

On motion duly made and seconded, minutes of the 516th meeting of the Council, held December 11, 1965, were approved as distributed.

#### 3. *Membership*

(a) On motion duly made and seconded, three applicants were voted election to Associate Membership. These were: Walter C. Rogers, Los Angeles County; Bennett F. Markel, Alameda-Contra Costa; William A. Cooper, Santa Clara County.

(b) On motion duly made and seconded, 19 members were voted election to Retired Membership. These were: Thomas I. Buckley, William R. Hirst, Alameda-Contra Costa County; Vincent Bonfiglio, Max L. Busch, Louis Felsen, Dorothy M. Franklin, Dorothy Hewitt, Wybren Hiemstra, Miriam Hubbell, S. Malcolm Magarian, Mary A. McConaughy, Richard F. Mogan, Albert J. Scholl, John E. Stoll, Kenneth H. Sutherland, Rex F. Swartz, Los Angeles County; Mary E. Mathes, San

Francisco County; David L. Reeves, Santa Barbara County; Fred A. Shore, Ventura County.

(c) On motion duly made and seconded, a reduction of dues was voted for 26 members for reasons of prolonged illness or postgraduate education.

#### 4. *Component Society Officers Conference*

Doctor L. Morgan Boyers, chairman of the 1966 Conference of Component Society Officers, reported on the one-day conference held the previous day in the same hotel. Approximately 350 society leaders and guests attended the program which was devoted to Public Laws 89-97 and 89-239. Doctor Boyers will submit a detailed report to the Council at its February meeting.

#### 5. *Commission on Hospital Affairs*

Doctor Bert Halter presented a document entitled, "Proposed Statement on Medical Staffing in County Hospitals." The statement, according to Doctor Halter, resulted from the contemplated changes brought about by Assembly Bill 5 and other developments. Doctor Halter suggested an amendment to the statement which pertained to collection of medical fees.

**ACTION:** *Voted to accept as policy the amended statement on "Medical Staffing in County Hospitals."*

#### 6. *Report of the President*

President Teall reported on his visits to county societies; announced that he had been named vice-chairman of the California Committee on Heart Disease, Cancer, and Stroke; discussed the "public hearings" on the Cal-Med plan which were held in Sacramento, January 8 and 10; reported on the January 15 meeting of the Task Force on Public Law 89-97.

#### 7. *Committee for Emergency Action*

President Teall reported that the Committee for Emergency Action had taken two actions since the last meeting of the Council. One involved the appointment of Doctor Carl Anderson to a small committee developing some ideas for implementation of Assembly Bill 5. The second was the designation of Doctor Leo Snyder to investigate the availability of medical care for workers in the Delano area.

**ACTION:** *Voted to affirm actions taken by the Committee for Emergency Action.*

#### 8. *Task Force on Public Law 89-97*

The Task Force met on January 15 and spent most of its time discussing the CMA Guidelines

for Utilization Review, according to President Teall. Several members of the Task Force had suggestions for changes in the guidelines. The Task Force recommended to the Council that the booklet be amended and that further distribution be decided by the Council itself.

**ACTION:** *Voted to make the suitable amendments in the "Guidelines for Utilization Review."*

**ACTION:** *Voted that the amended document be released to any organization requesting it. (It is understood that cost reimbursement will be expected on "large quantity" orders.)*

The Task Force also reviewed the developments under P.L. 89-97 with regard to hospital-based physicians. A recommendation was passed that the recently announced "Principles for Reimbursement under Medicare for Hospital-Based Physicians"—released by the Social Security Administration—be distributed to pathologists and radiologists throughout California.

**ACTION:** *Voted to distribute the statement to radiologists and pathologists in California (members of CMA) and invite their reactions.*

#### 9. Committee on Committees

President-Elect MacLaggan reported several recommendations of the Committee on Committees:

—That Doctor John E. Affeldt of Los Angeles be designated as CMA representative to a Public Health Department advisory committee for the implementation of a program of residential care of the mentally normal/physically handicapped.

—That three names be submitted to serve on a State Department of Education advisory committee on courses for medical assistants. The three names are Doctors Charlotte Baer of San Francisco, Leon O. Burke of Sacramento, and John B. deC. M. Saunders of San Francisco.

—That 12 names be submitted to the State Department of Social Welfare for its advisory committee on Ophthalmology (CMA has been asked to submit 12 names, six of whom will be chosen). The names recommended are: Doctors Robert Tour of San Francisco, Ernest Denicke of San Rafael, Karl Chiapella of Chico, Herman A. Iverson of Eureka, Frank Winter of Palo Alto, Daniel Vaughan of San Jose, Gilbert Reese of Sacramento, Harold Alexander of Santa Barbara, George Tabor of San Diego, Robert Shearer of Glendale, Robert Hopkins of Stockton, Milton Van Riesen of Palo Alto. These are in addition to the six persons currently serving. (If Doctor Jam-

polski is not on the current list, the committee recommended that his name be added.)

**ACTION:** *Voted to approve the recommendations of the Committee on Committees.*

#### 10. Medical Care Project in Watts

Doctor Roger Egeberg, dean of the USC medical school, informed the Council of his school's participation in an effort to improve the quality, scope and availability of medical care in the Watts area of southeast Los Angeles. This project (which would involve the construction of a hospital facility, plus social services) is being undertaken at the request of the Office of Economic Opportunity. He requested CMA assistance in the implementation of the program.

#### 11. Affiliated Organizations and Invited Guests

Representatives of several organizations and departments of state government reported on activities of interest to the medical profession. No action was required. Among those present were Doctor Lester Breslow, director of the Department of Public Health; Mr. Charles Jackson, president-elect of the California Hospital Association; and Doctor William Steinmetz, president of the California Veterinary Medical Association.

#### 12. California Physicians' Service

Doctor William Thompson, board chairman, reported on several steps CPS has taken to prepare for its possible role under the new governmental medical care programs. These steps include: appointment of an ad hoc trustee committee on government programs with Doctor Richard Wilbur as chairman, realignment of some staff personnel to handle the new programs, appointment of consultants in electronic data processing, approval to join with two Blue Cross plans in having Mr. William Whelan act as coordinator for all three in dealing with the State on Assembly Bill 5, development of guidelines for utilization and fee review to help county societies (this is being done in cooperation with Council members and executive secretaries).

#### 13. Technical Advisory Committee to State Department of Finance

A full report on the activities of the technical advisory committee to the State Department of Finance was presented by Doctor Maurice S. Salomon, CMA representative. He reported that the State Department of Finance has agreed to utilize the "current edition of the Relative Value Studies."



#### 14. Finance Committee

Doctor Harold Kay presented a draft of the proposed budget for the 1966-67 fiscal year. As originally drafted, the budget shows a deficit of nearly \$135,000. This assumes current programs are continued and dues remain at the same level. Expansion of activities, committees and personnel would require additional expenses and a dues increase, Doctor Kay noted. Final Council action on the budget is due in February; the House of Delegates will receive the Council recommendations in March. Doctor Kay requested approval to delete \$3,000 (from the proposed 66-67 budget) for the California Committee on Nurse Recruitment.

**ACTION:** *Permission granted to delete the \$3,000 item from the budget.*

Inasmuch as the Joint Commission on the Accreditation of Hospitals will assume the role of accrediting nursing homes, Doctor Kay asked for permission to cease any further support of the California Commission on Accreditation of Nursing Homes.

**ACTION:** *Voted approval of Doctor Kay's recommendation.*

#### 15. Commission on Community Health Services

Doctor Harold Kay reported several recommendations of the Committee on Automotive and Traffic Safety:

—That the CMA support again the "presumptive limits and "implied consent" bills if and when the Governor places them before the Legislature.

—That CMA urge the Department of Motor Vehicles to discontinue its plan of putting blood types on drivers' licenses.

—That CMA support legislation which would require operators of two-wheeled motor vehicles to wear protective headgear, of an approved type, whenever operating said vehicles.

—That CMA support legislation requiring that inter-city busses (regardless of the number of seats) be equipped with seat belts as called for in Resolution No. 5-65.

**ACTION:** *Voted to approve all of these recommendations.*

#### 16. Medical Care in Impoverished Areas

Doctor Harold Kay asked for Council permission to allow the Committee on Rural Health to meet with the "Student Medical Conference," an organization of students interested in the provision

of medical care to low-income workers, particularly in the rural areas of the Central Valley.

**ACTION:** *Permission granted to the Committee on Rural Health.*

#### 17. Bureau of Research & Planning

Doctor Elmer Gooel, reporting for Chairman Sherman, told of several projects presented at the 14 January meeting of the Bureau.

After hearing from Doctor Charles Peck of Sonoma County and Robert Furlong, a special consultant to the Assembly Judiciary Committee, the Bureau voted to recommend to the Council that an ad hoc committee be appointed to consult with the Assembly Judiciary Committee on problems of "family disintegration."

**ACTION:** *Voted approval of a small ad hoc committee (Chairman Anderson to make the appointments.)*

The Bureau recommended that CMA "co-sponsor" a meeting in Orange County of the Instrument Society of America.

**ACTION:** *Voted to give supporting publicity to the convention and to co-sponsor the program.*

In a detailed report on Resolution No. 4-65 (Discontinuity of Coverage), the Bureau recommended "that the CMA Commission on Medical Services, in addition to its continuing liaison with the insurance industry, discuss this problem (4-65) with trade and labor associations and organizations and, if feasible, develop a register whereby specific complaints can be received with individual physicians wherever such instances of discontinuity occur. Grievance and other committees within the structure of county medical societies should also become involved in providing information as part of a complaint register."

**ACTION:** *Voted to refer the problem to the Commission on Medical Services with the Bureau recommendations.*

Resolution No. 50-65 called for a correction in the imbalance of appropriations to research and practicing physician education. The Bureau believes that, to a large degree, this issue is gradually being resolved, and that no further action is necessary at this time.

**ACTION:** *Voted concurrence with the statement of the Bureau on this resolution.*

#### 18. Committee on Legislation

Doctor Dan Kilroy previewed the coming election for Assembly and Senate seats, announced that he expected some parts of Assembly Speaker Jesse Unruh's Cal-Med program to be placed be-

fore the Legislature, described the dates for the budget session, and suggested that CMA watch for amendments to the Casey Bill.

#### 19. *Proposed Amendments to the CMA Constitution and Bylaws*

A number of proposed amendments to the Constitution and Bylaws of the Association were described by Messrs. Hassard and Whelan upon request by Chairman Anderson. The changes will be recommended to the House of Delegates by the Council. The amendments concern composition of the Council, officers, classes of membership, termination or suspension of membership, duties of district councilors, employment and duties of staff personnel, and others.

**ACTION:** *Voted to approve submission of the Constitution and Bylaw amendments, as amended. Staff was requested to prepare them in suitable form.*

#### 20. *Scientific Board*

Doctor Edward B. Shaw offered a recommendation of the Scientific Board that a Committee on Cardiovascular Disease be established, consisting of approximately five members.

**ACTION:** *Voted to establish a Committee on Cardiovascular Disease.*

#### *Adjournment*

There being no further business to come before it, the meeting was adjourned at 4:40 p.m. in memory of Arthur Kirchner, M.D.

CARL E. ANDERSON, M.D., *Chairman*  
MATTHEW N. HOSMER, M.D., *Secretary*

## Acute Cardiac Care

### *The Role of the Registered Nurse*

A joint statement by the California Medical Association, the California Hospital Association and the California Nurses' Association.

IT HAS BEEN DEMONSTRATED that a significant reduction in mortality from acute myocardial infarction can be achieved by establishing specialized coronary care units within those hospitals which have the capabilities, equipment and trained personnel to provide such care.

It is recognized that intensive observation, and immediate recognition of the patient's needs are essential. Institution of appropriate life-saving therapy must be done within an extremely short space of time.

With the intent of promoting good patient care and protecting the doctor, the nurse and the hospital, the California Medical Association, the California Hospital Association and the California Nurses' Association recognize the propriety of registered nurses to use monitoring, defibrillation, and resuscitative equipment, and to institute immediate life-saving corrective measures, if a licensed physician is not immediately available to

do so and all the following conditions exist:

1. The registered nurse has had special competent instruction in the techniques, and

2. The registered nurse performs the authorized procedures upon: (a) the direct order of a licensed doctor of medicine, or (b) pursuant to standing procedures established as set forth in item 4 following.

3. Where a hospital has determined that a registered nurse may perform the techniques, then the techniques to be performed within the framework of designated preparation and practice of the nurse shall be established for the hospital by a committee composed of representatives from the medical staff, the department of nursing, and the administration. This framework of preparation and practice shall be reproduced in writing and made available to the total medical and nursing staffs.

4. Such criteria shall make provision that in case of a cardiac emergency, a licensed physician and other designated categories of personnel are to be immediately summoned to assist the registered nurse who is carrying out the physician's orders, or is carrying out standing procedures established by the medical staff of the hospital, and contained in the adopted criteria.

**The Committee on Occupational Health has prepared a statement on Medical Supervision of Organic Phosphate Pesticide Workers which will be published in the April issue. Anyone who wishes a copy of it before that time may obtain one by writing to the California Medical Association, 693 Sutter Street, San Francisco, California 94102.**



## In Memoriam

BEARDSLEY, JOHN R., San Diego. Died 22 January 1966, in San Diego, aged 60. Graduate of Loyola University School of Medicine, Chicago, Illinois, 1931. Licensed in California in 1932. Doctor Beardsley was a member of the San Diego County Medical Society.



BECK, JOSEPH KARL, Newport Beach. Died 26 January 1966, by drowning, aged 72. Graduate of Jefferson Medical College of Philadelphia, Pennsylvania, 1919. Licensed in California in 1937. Doctor Beck was a retired member of the Riverside County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



COOPER, GILBERT O., Los Angeles. Died 10 October 1965, near Medicine Bow, Wyoming, aged 58, of heart disease. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1935. Licensed in California in 1935. M.D. degree from California College of Medicine, 1962. Doctor Cooper was a member of the Forty First Medical Society.



CREVER, JAMES WILLIS, JR., Susanville. Died 29 December 1965, in Susanville, aged 57. Graduate of Stanford University School of Medicine, Palo Alto-San Francisco, 1934. Licensed in California in 1934. Doctor Crever was a retired member of the Lassen County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



CULLEN, EDWARD R., Long Beach. Died 22 January 1966, in Long Beach, aged 55, of myocardial infarction. Graduate of the University of Southern California School of Medicine, Los Angeles, 1941. Licensed in California in 1941. Doctor Cullen was a member of the Los Angeles County Medical Association.



HERON, IVAN C., San Francisco. Died 29 January 1966, in San Francisco, aged 70. Graduate of Stanford University School of Medicine, Palo Alto-San Francisco, 1923. Licensed in California in 1923. Doctor Heron was a member of the San Francisco Medical Society.



HIPPACH, ROSCOE MARTIN, Yucaipa. Died 30 January 1966, aged 72. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1923. Licensed in California in 1923. Doctor Hippach was a member of the San Bernardino County Medical Society.



JONES, F. HARRIMAN, Long Beach. Died 22 January 1966, in Long Beach, aged 54, of pulmonary edema.

Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1937. Licensed in California in 1937. Doctor Jones was a member of the Los Angeles County Medical Association.



LANGSTROTH, LOVELL, San Francisco. Died 19 January 1966, aged 85. Graduate of Cooper Medical College, San Francisco, 1912. Licensed in California in 1912. Doctor Langstroth was a retired member of the San Francisco Medical Society and the California Medical Association, and an associate member of the American Medical Association.



LOWERY, VINCENT EDWARD, San Francisco. Died 24 January 1966, in Belvedere, aged 41. Graduate of the University of Southern California School of Medicine, Los Angeles, 1948. Licensed in California in 1952. Dr. Lowery was a member of the San Francisco Medical Society.



MACDONALD, FRANCIS B., Livermore. Died 16 January 1966, in Oakland, aged 66, of carcinoma of stomach. Graduate of Long Island College of Medicine, 1925. Licensed in California in 1945. Doctor MacDonald was a member of the Alameda-Contra Costa Medical Association.



NIELSEN, CEDRIC A., Camarillo. Died 5 February 1966, aged 53. Graduate of Washington University School of Medicine, St. Louis, Missouri, 1941. Licensed in California in 1957. Doctor Nielsen was a member of the Ventura County Medical Society.



OUER, ROY ALEXANDER, San Diego. Died 6 February 1966, aged 56. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1936. Licensed in California in 1936. Doctor Ouer was a member of the San Diego County Medical Society.



ROBINSON, PAUL TIMOTHY, Richmond. Died 1 February 1966, in San Francisco, aged 69. Graduate of Meharry Medical College, Nashville, Tennessee, 1931. Licensed in California in 1953. Doctor Robinson was a member of the Alameda-Contra Costa Medical Association.



RUTH, GERHARD DANIEL, Los Angeles. Died 3 February 1966, in Los Angeles, aged 84, of acute coronary thrombosis. Graduate of the University Medical College of Kansas City, Missouri, 1907. Licensed in California in 1919. Doctor Ruth was a member of the Los Angeles County Medical Association.



SALISBURY, HARRY ROBERT, Burbank. Died 24 January 1966, in Burbank, aged 59, of heart disease. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1936. Licensed in California in 1936. M.D. degree from California College of Medicine, 1962. Doctor Salisbury was a member of the Los Angeles County Medical Association.



SPOMER, ISAAC, Tulelake. Died 17 December 1965, aged 58. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1941. Licensed in California in 1942. Doctor Spomer was a member of the Siskiyou County Medical Society.



STOLL, JOHN E., Monrovia. Died 14 January 1966, in Monrovia, aged 65, of heart disease. Graduate of Rush

Medical College, Chicago, Illinois, 1925. Licensed in California in 1931. Doctor Stoll was a member of the Los Angeles County Medical Association.



WINKLER, RALPH KENNETH, Stockton. Died 12 January 1966, in Stockton, aged 43. Graduate of Washington University School of Medicine, St. Louis, Missouri, 1945. Licensed in California in 1946. Doctor Winkler was a member of the San Joaquin County Medical Society.



WINTER, WILLIAM GORDON, Fresno. Died 8 January 1966, aged 62. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1933. Licensed in California in 1933. Doctor Winter was a member of the Fresno County Medical Society.





# 16th annual redwood regional conference

**KONOCTI HARBOR INN**  
*Clear Lake*  
*April 28-30, 1966*

Presented cooperatively by North Coast Counties Medical Societies, University of Southern California School of Medicine, and the Committee on Continuing Medical Education, California Medical Association. A 12-hour course.

**HOST: Sonoma County Medical Society.**

**Regional Chairman: Lucius L. Button, M.D.,**  
1102 Montgomery Drive, Santa Rosa.

**CONFERENCE FEE: \$15.00.** For additional information contact Continuing Medical Education office, California Medical Association, 693 Sutter Street, San Francisco 94102. All California Medical Association members and their families are cordially invited to attend.

## PROGRAM TOPICS: CARDIOLOGY... HYPERTENSION... OBESITY... DIABETES... ORAL CONTRACEPTION... MEDICAL INTERVIEWING

### THURSDAY, APRIL 28

12:30—Registration

#### *Afternoon Session*

- 2:00—The Hypertensive Workup—Edward D. Freis, M.D.
- 2:30—Therapy of Congestive Failure—George C. Griffith, M.D.
- 3:00—Obesity—Donald W. Petit, M.D.
- 3:45—CONCURRENT WORKSHOPS (you may go to one of your choice):
  - A. Diabetes—Robert E. Tranquada, M.D.
  - B. Psychiatric Interviewing—Allen J. Enelow, M.D.
  - C. Hypertensive Workup—Edward D. Freis, M.D., Robert F. Maronde, M.D.

### FRIDAY, APRIL 29

#### *Morning Session*

- 9:00—Therapy in Hypertension—Edward D. Freis, M.D.
- 9:30—Panel on Therapy of Myocardial Infarction—David H. Blankenhorn, M.D., George C. Griffith, M.D., Phil R. Manning, M.D.
- 10:45—CONCURRENT WORKSHOPS (you may go to one of your choice):
  - A. Cardiovascular Disease—David H. Blankenhorn, M.D.
  - B. Diabetes—Robert E. Tranquada, M.D.
  - C. Psychiatric Interviewing—Allen J. Enelow, M.D.

- 12:00—Luncheon (for Doctors and their wives)  
Lewis H. Lambert, M.D.

#### *Afternoon Session*

- 1:30—Pharmacology of Antihypertensive Drugs—Robert F. Maronde, M.D.
- 2:00—Family Planning Method—Gordon P. Griggs, M.D.
- 2:45—CONCURRENT WORKSHOPS (you may go to one of your choice):
  - A. Cardiovascular Disease—David H. Blankenhorn, M.D., George C. Griffith, M.D., Phil R. Manning, M.D.
  - B. Hypertension—Robert F. Maronde, M.D.
  - C. Problems of Obesity—Donald W. Petit, M.D.

### SATURDAY, APRIL 30

#### *Morning Session*

- 9:00—The Prevention, Recognition and Management of Pulmonary Emboli—George C. Griffith, M.D.
- 9:30—Induction of Ovulation—Gordon P. Griggs, M.D.
- 10:00—Newer Tests of Thyroid Function—Donald W. Petit, M.D.
- 10:45—CONCURRENT WORKSHOPS (you may go to one of your choice):
  - A. Cardiovascular Disease, George C. Griffith, M.D., Phil R. Manning, M.D.
  - B. Thyroid Disease—Donald W. Petit, M.D.
  - C. Psychiatric Interviewing—Allen J. Enelow, M.D.

*For complete program see February issue*



# ANNUAL SCIENTIFIC ASSEMBLY

**MARCH 19-23, 1966\***

**LOS ANGELES**

*current concepts in therapy*

**POINT AND COUNTERPOINT**

*featuring—*

**RENAL FAILURE  
CORONARY ARTERY DISEASE  
GASTROINTESTINAL HEMORRHAGE**

- *among the distinguished speakers  
presenting their “current concepts in therapy”:*

- CHARLES K. FRIEDBERG, M.D., Columbia University
- BERNARD LOWN, M.D., Harvard University
- BELDING H. SCRIBNER, M.D., University of Washington
- OWEN H. WANGENSTEEN, M.D., University of Minnesota

A VARIETY OF EVENTS in addition to those directly related to this year's theme WILL HIGHLIGHT YOUR 1966 ANNUAL SCIENTIFIC ASSEMBLY . . . eighteen medical specialty section meetings . . . seven special conferences . . . motion picture symposia . . . color TV programs . . . scientific and technical exhibits.

\*House of Delegates and Special Conferences start Saturday, March 19.



# Voluntary Health Insurance Coverage in California, 1952 to 1963

## A Report of the Bureau of Research and Planning, California Medical Association

■ *More than seven out of every ten of an estimated civilian population of 17.3 million people in California were covered under some form of voluntary health insurance at the close of 1963.*

*Between 1952 and 1963, the number of Californians covered for hospital expenses increased from 5.7 million to 12.3 million; for surgical expenses from 5.4 million to 11.6 million; and for regular medical expenses from 3.0 million to 10.1 million.*

*The percentage covered by health insurance also rose significantly: for hospitalization, from 51.3 to 71.0 per cent; for surgical, from 48.2 to 67.1 per cent; and for regular medical from 27.2 to 57.9 per cent. The rate of increase in hospitalization coverage was slightly higher in California than in the total U.S.; however, the per cent of persons covered remains lower. For surgical coverage, both the rate of increase and the per cent covered are lower in California. For regular medical, growth rates in California and in the U.S. were similar, however the over-all per cent covered is significantly higher in California.*

*Major medical coverage, which has shown the fastest growth rate, covered only 0.4 per cent of the U.S. population in 1952 and 17.1 per cent by the end of 1963. Comparable figures for California are not available.*

THE PERIOD BETWEEN 1952 and 1963 was a period of dramatic growth for voluntary health insurance coverage in both California and the total United States. At the end of 1963, approximately 12,310,000 people, or slightly over 70 per cent of an estimated civilian population of 17,349,000 people in California,\* were covered under some

form of voluntary health insurance. This is more than twice the number of persons insured in 1952 and about four hundred thousand more than the number insured the previous year.

Within these 12 years, the number of persons covered for hospital expenses increased by 6.57 million in California and by 53.66 million in the total United States. The increases for surgical insurance coverage were 6.24 million in California and 61.75 million in the United States. For regular medical coverage the increases were 7.0 mil-

Sources: California Department of Finance, Budget Division, California Population—1964; Health Insurance Council, The Extent of Voluntary Health Insurance Coverage, Annual Surveys 1953-1963; Health Insurance Council, Accident and Health Insurance Coverage in the United States, 1952.

\*Civilian population estimate as of 1 July 1963.

TABLE 1. *Number of Persons Covered for Hospital, Surgical, Regular Medical, and Major Medical Expenses, California and the United States, 1952-1963*

Year	Number of Persons Covered (in millions)							
	Hospital		Surgical		Regular Medical		Major Medical <sup>1</sup>	
	Calif.	U.S.	Calif.	U.S.	Calif.	U.S.	Calif. <sup>2</sup>	U.S.
1952	5.74	91.67	5.40	73.16	3.05	35.80	0.04	0.69
1953	6.46	98.79	6.35	82.35	4.50	42.91	0.09	1.22
1954	6.74	101.49	6.17	85.89	4.30	47.25	0.17	2.24
1955	7.10	107.66	6.56	91.93	5.06	55.51	0.41	5.24
1956	7.77	115.95	7.91	101.32	6.40	64.89	0.70	8.88
1957	9.14	121.43	8.86	108.93	6.78	71.81	0.82	10.12
1958	9.45	123.04	9.18	114.44	7.25	75.40	1.01	12.22
1959	9.89	127.90	9.56	116.94	7.84	82.62	1.30	15.40
1960	10.75	131.96	10.27	121.05	8.56	87.54	1.67	19.12
1961	11.17	135.04	10.71	125.30	9.06	92.63	2.21	24.90
1962	11.95	141.44	11.30	131.18	9.54	98.20	2.59	28.50
1963	12.31	145.33	11.64	134.91	10.05	102.18	2.97	31.99

<sup>1</sup>Data from 1952-1956 includes persons with supplementary or comprehensive plans; data from 1957-1963 includes only those with supplementary plans.

<sup>2</sup>Data are estimated and are based on the assumption that the percentage of California's population covered for major medical expenses is the same as that of the U.S. population.

lion in California and 66.38 million in the United States. Major medical coverage in the United States experienced a gain of 31.30 million which was also the largest percentage increase—the 1963 figure is more than 45 times as great as the 1952 figure—among any of the various types of insurance coverage.

Table 1 shows numbers of persons in California and in the total United States, from 1952 to 1963, who had coverage for hospital, surgical, regular medical and major medical expenses. The number of Californians covered for hospital expenses has increased steadily during the 12-year period from 1952 (5.7 million) to 1963 (12.3 million). The greatest increase for any one-year period, occurring between 1956 and 1957, was 1.37 million.

Prepayment and insurance coverage for surgical expenses has also shown a steady increase with the exception of the one period between 1953 and 1954. The greatest increase during any one-year

period was in 1956 when the number of persons covered for surgical expenses rose by 1.35 million persons.

Prepayment and insurance for regular medical expenses shows a pattern of growth similar to that for surgical coverage. There was also a decrease in the number of persons covered under this type of insurance between 1953 and 1954—a decrease of some 200,000 persons. The greatest increase, however, occurred between 1952 and 1953, not in 1956 as had been the case in coverage for surgical expenses. The number of persons protected for regular medical expenses increased by 1.45 million persons in that one-year period.

Major medical coverage will be discussed in a later section of this report.

Table 2 shows the percentage of the California population and of the United States population covered for various types of expenses between 1952 and 1963.

TABLE 2. *Percentage of Population Covered for Hospital, Surgical, Regular Medical, and Major Medical Expenses, California and the United States, 1952-1963.*

Year	Hospital		Surgical		Regular Medical		Major Medical	
	Calif.	U.S.	Calif.	U.S.	Calif.	U.S.	U.S. <sup>1</sup>	
1952	51.3%	59.6%	48.2%	47.5%	27.2%	23.3%	0.4%	
1953	55.3	63.1	54.4	52.6	38.5	27.4	0.8	
1954	55.4	63.6	50.7	53.8	35.3	29.6	1.4	
1955	56.0	66.1	51.8	56.4	39.9	34.1	3.2	
1956	58.7	69.8	59.7	61.0	48.3	39.1	5.3	
1957	66.0	71.8	64.0	64.4	49.0	42.5	5.9	
1958	65.6	71.4	63.7	66.4	50.3	43.8	7.0	
1959	66.1	73.0	63.9	66.7	52.4	47.1	8.7	
1960	69.1	74.1	66.0	67.9	55.0	49.1	10.7	
1961	69.1	74.5	66.3	69.1	56.1	51.1	13.7	
1962	71.4	77.0	67.5	71.4	57.0	53.4	15.5	
1963	71.0	77.9	67.1	72.3	57.9	54.8	17.1	

<sup>1</sup>Percentage Coverage by State not Available.



Prior to 1958 the United States had experienced an irregular growth pattern in hospital expense coverage; during some years (1953, 1955 and 1956) there were substantial increases in the percentage of population covered for hospital expenses; during others (1954 and 1957) minimal increases or decreases occurred. Since 1958, however, the growth of hospital coverage has been slight but steady. Almost every year finds between 1 and 2 per cent more of the population in the total United States insured for hospital benefits. California's profile has been somewhat erratic throughout the 12 years. Changes in percentage of population covered have been as great as the 7.3 per cent increase shown during one year (1957) to a 0.4 per cent decrease shown during two other years (1958 and 1963).

While each year shows that the percentage of Californians covered by this type of voluntary health insurance is less than that of the total United States population, the gap in coverage rates has been narrowing during the past 12 years. The increase in the rate of coverage amounted to 38.4 per cent in California and to 30.7 per cent in the United States.

The percentage of population covered for surgical expenses for both California and the total United States is also indicated in Table 2. Significant increases in surgical coverage took place between 1952 and 1957. During these five years the percentage of the total United States population with surgical coverage shows a steady increase and, with the exception of 1954, when it amounted to 1.2 per cent, the average annual gain was more than 2.5 per cent of the total population. Since 1957, however, increases have been smaller (less than 2.0 per cent each year) and more consistent. Unlike the United States, which showed no decreases whatsoever, the pattern in California shows substantial year-to-year variations, both upward (6.2 per cent in 1953) and downward (3.7 per cent in 1954).

Between 1955 and 1957 great strides were made in surgical insurance coverage of Californians, with a total two-year gain of over 12 per cent of the population. Since 1957, however, surgical coverage in California has been growing at a much slower pace so that the gap between the percentage of United States population covered has gradually increased until 1963 when a disparity of 4.5 percentage points in the rate of coverage existed.

The percentage coverage in California was slightly greater than that of the total United States in 1952 and 1953. Since that time, however, coverage has been less prevalent at the State level than on the national level, with the result that within the 12-year period, the coverage rate in the total United States has increased 52.2 per cent while in California the increase was 39.2 per cent.

Between 1952 through 1956 regular medical insurance coverage grew more rapidly than in the more recent years. Nationally, annual percentage increases range between 2.2 per cent (1954) and 5.0 per cent (1956). Since 1957, with the exception of 1959, the annual percentage increases have been considerably less substantial. In no case, however, was there a decrease in the per cent of the population covered.

While the United States shows a consistent rise in percentage coverage each year, California shows marked increases in certain years, less spectacular increases in other years, and a decrease in one year, 1954. An irregular growth pattern of coverage between 1952 and 1956 gave way to a more uniform pattern between 1956 and 1963. During these years, the annual percentage increase in coverage ranged between 0.7 per cent (1957) and 2.6 per cent (1960).

A greater percentage of the California population was insured for regular medical expense benefits than was the case in the total United States. The over-all growth pattern of regular medical insurance for both California and the total United States, however, is very similar. During this 12-year period, the rate of coverage increased 113 per cent in California and 135 per cent in the United States.

Regular medical expense coverage was more widespread in California than in the total United States between 1952 and 1963. Each single year shows that the percentage of Californians covered by this type of insurance was somewhat higher than the percentage of the total United States population. The gap, however, is narrowing and in 1963 amounted to a scant 3.1 per cent.

Lastly, Table 2 shows the percentage of the United States population covered for major medical expenses between 1952 and 1963. The data shown for 1952 through 1956 include those persons with either *supplementary* or *comprehensive* prepayment and insurance. Since comprehensive major medical expense insurance encompasses basic plan protection, the number of persons so

protected are included in the hospital, surgical, or regular medical expense coverage figures (as applicable) given for these years (1952-1956) as well as under "major medical." Since 1957, however, the data shown include only those persons with *supplementary* protection. This alteration in recording procedure accounts for the relatively slight increase shown in 1957.

Major medical insurance is the fastest growing type of voluntary health insurance in the United States. In 1952, only 0.4 per cent of the total United States population were covered for major medical expenses; by the end of 1963, after substantial increases in coverage each year, approximately 17.1 per cent of the civilian population had such protection. Hence, over 45 times as many persons in the United States were insured for major medical benefits in 1963 than in 1952. In California, however, over 74 times as many persons were covered by this type of voluntary health insurance in 1963 than in 1952. The discrepancy between the rates of increase in coverage in California and the rates in the United States is due to the faster rate of population growth in California.

Unfortunately, major medical insurance coverage data are not available for individual states. However, if one can assume that the percentage of Californians protected is approximately the same as that of the total United States population, certain estimates can be made. It can therefore be estimated that about 40,000 Californians were protected by major medical insurance policies in 1952 and almost three million persons by 1963.

Table 3 compares data on the percentage increase in California's civilian population with numbers and per cents of increase in persons covered by hospital, surgical, and regular medical pre-

payment and insurance between 1952 and 1963.

While hospital coverage did not experience any year-to-year decreases, its growth during 1958 and 1963 was at a slower rate than that of the population. In 1958, California's population increased by 4.1 per cent and coverage by 3.3 per cent; in 1963, the population increased by 3.7 and the coverage by 3.1 per cent. The greatest relative gains in coverage were in 1952, 1953 and 1957 when population increased by 4.1 per cent, 4.4 per cent and 4.5 per cent, and coverage increased by 12.5 per cent, 12.7 per cent and 17.7 per cent, respectively.

Surgical coverage, on the other hand, experienced a net increase during a one-year period. In 1954, there was a 2.9 per cent decrease in coverage while the population increased by a 4.2 per cent. In 1958, surgical coverage increased by 3.6 per cent while the population increased by 3.1 per cent, and in 1963, coverage increased by 3.0 per cent and population by 3.7 per cent. In 1953 and 1956, however, population increased by 4.4 per cent and 4.6 per cent and surgical insurance coverage increased by 17.8 per cent and 20.3 per cent, respectively; these were the two largest annual percentage increases in surgical insurance coverage.

A more spectacular growth pattern is shown for regular medical coverage. In 1952, 1953 and 1956, while the percentage increases in California's population were 4.1, 4.4 and 4.6, the percentage increases in regular medical coverage were 29.8, 47.6 and 26.3, respectively. With the exception of 1954, when California's population increased by 4.2 per cent and regular medical coverage decreased by 4.3 per cent, this type of coverage has consistently grown at a rate faster than the state's population.

On the whole, voluntary health insurance cov-

TABLE 3. *Percentage Increase in Population and Number and Percentage Increase in Number of Persons Covered by Hospital, Surgical, and Regular Medical Prepayment Insurance, in California, 1952-1963*

Year	Percentage Increase in California's Population	Number and Percentage Increase in Coverage					
		Hospital		Surgical		Regular Medical	
		No. (000 omitted)	%	No. (000 omitted)	%	No. (000 omitted)	%
1952	4.1	636	12.5	958	9.9	699	29.8
1953	4.4	726	12.7	486	17.8	1,450	47.6
1954	4.2	276	4.3	—184	—2.9	—195	—4.3
1955	4.0	359	5.3	391	6.3	761	17.7
1956	4.6	675	9.5	1,335	20.3	1,332	26.3
1957	4.5	1,372	17.7	954	12.1	390	6.1
1958	4.1	303	3.3	318	3.6	463	6.8
1959	3.8	444	4.7	387	4.2	589	8.1
1960	4.0	862	8.7	705	7.4	722	9.2
1961	3.8	418	3.8	442	4.3	506	5.9
1962	3.6	776	6.9	587	5.8	478	5.3
1963	3.7	366	3.1	343	3.0	511	5.4



erage has more than kept up with California's population increases.

Since the foregoing figures and per cents are gross estimates and do not represent an evaluation of coverage in terms of an available market for voluntary health insurance, perhaps a few comments are in order to place the data in somewhat finer perspective. Aside from those persons, who, for personal reasons, do not desire voluntary health insurance coverage, a significant per cent of those not involved under voluntary health insurance coverage are provided with health care services, or have such services financed for them. These would include—but are not limited to—persons eligible for care through the U.S. Public Health Service, such as American seamen; those persons eligible for care such as veterans whose care in many cases is for non-service-connected conditions; persons who receive care under vocational rehabilitation; people eligible for care under

California's Public Assistance Medical Care and Medical Assistance to the Aged Programs, Armed Forces personnel and dependents covered in the Medicare program of the Department of Defense, the services provided under the Crippled Children's Program administered by the State Department of Public Health; and last but not least, persons who have no other type of coverage but who are not covered by Disability Insurance Hospitalization Benefits, administered by the State Department of Employment.

It is estimated that between 40 per cent to 50 per cent of the remaining five million persons in California in 1963 not covered by voluntary health insurance have some other type of health care protection. Thus, a higher per cent of the population in California has health care service programs available to them than is reflected just in the enrollment under voluntary health insurance programs.

693 Sutter Street, San Francisco, California 94102.



# LETTERS *to the Editor*

## The Function of the Well Man Clinic

LEWIS T. BULLOCK, M.D.

WE ARE DEVOTED to the identification of the community action which is most needed for the control of heart disease, cancer and stroke. The second and third were added, I think, by the President's Commission following the Second National Heart Conference. I will add some other concerns.

A large amount of cud chewing and grinding of old grist is inevitable in a meeting of this sort. What we need is the identification of a new field in which available knowledge is not being applied. We must recognize that community mobilization will not solve the problems of heart disease, high blood pressure or cancer. This requires the availability of knowledge which we do not have. The Heart and Cancer Societies are doing a fine job in promoting the research required to develop such knowledge. But there is a large area in which community mobilization would result in the application of available knowledge where it is not now being applied.

Proper control of heart disease, high blood pressure, diabetes, cancer, tuberculosis, arteriosclerosis and resulting stroke requires early identification. The value of preventive medicine in pediatrics is well recognized and well baby clinics are widespread. It is not clear why an infant is considered to be so much more valuable than a man or a woman.

Industry clearly recognizes the value of regular annual examinations by the very many programs making this available to executives. If improving the health and prolonging the life of an executive is of value to industry, why isn't improving the health and prolonging the life of citizens of value to the community?

Presented at California Follow-up Conference of the Second National Conference on Cardiovascular Diseases, San Francisco, 3 December 1965.

The Cancer Society, the Heart Association, the Tuberculosis and Diabetes Associations have done an outstanding job of informing the community of the value of early detection and the importance of regular annual examinations. The public has responded and the concept of a regular annual medical checkup is widely accepted. It is not universal. All doctors do not respond to this need. But it is the standard of medical care which is accepted by the American Society of Internal Medicine and all of its member Internists. The Health Associations constantly advise the public to have regular examinations but for one group this is impossible and on them the message is lost.

I have studied many schedules of fees for medical care. I have not found one which lists—Regular Annual Preventive Examination. All insurance fee schedules suggest that people should be treated for far advanced diseases but should not be provided facilities for early diagnosis. There appears to be a need for a re-evaluation of objectives in this field.

Our County Hospitals have Outpatient Clinics for Heart Disease, Tuberculosis, Women's Diseases, High Blood Pressure, Cancer, Rectal Diseases and all the other various diseases but none for Preventive Medical Care. A nonsymptomatic citizen approaching a County Hospital Outpatient Clinic with a desire to determine if he has the early stages of cancer, high blood pressure, valvular heart disease, diabetes or tuberculosis is greeted with amazement. He is told—we have no Well Man Clinic. If he has congestive heart failure he is accepted. If he has metastatic cancer there is a place for him. If he has diabetic coma the County will treat him. But as far as I can determine there is not a single County Hospital in California with a Well Man Clinic.

Why do our communities wait for the symptoms of congestive failure before providing help for the indigent patient with heart disease? Why do our communities wait for the symptoms of metastatic cancer before providing assistance to



the indigent patient with malignancy? Why should we wait for coma before providing assistance to the indigent patient with diabetes? Why are the standards of care for the indigent so different from the standards widely accepted for other people? If the County is providing medical care for a certain group in the community, why shouldn't it provide the same type of preventive medicine available to the rest of the community?

Considering the importance of this service to the health of Americans it is astounding that Preventive Medical Care is specifically excluded from the services available under the Medicare Law. Like the Counties, the Government is apparently only interested in treating far advanced disease. This is an excellent illustration of how far the standards of Governmental Medical Care may be below the standards now accepted by the American Public.

Does your County Hospital have a Well Man Clinic? A Well Woman Clinic? If not, why not? This is the great hiatus in the services available for the control of heart disease, cancer and stroke. This is the need for community mobilization for the control of these diseases. Each one of you should return to your community and ask your Supervisors, "Do we have a Well Man Clinic, a Well Woman Clinic?" The answer will be no. If you want to mobilize your community for the control of heart disease, cancer and stroke, you must mobilize sufficient support in your area to produce a Well Man Clinic in your County Hospital Out-patient Department.

I wish to make it crystal clear that this hiatus in medical services is not the fault of the County Supervisors. It is my fault. It is your fault. We have not previously called this to the attention of the Supervisors. We have failed to establish adequate standards for the medical care of the indigent. But having centered our attention on this deficiency, we must all go back to our communities and insist that there be a Well Man Clinic for the early detection of heart disease, high blood pressure, cancer, diabetes and tuberculosis. Unless we do this we are failing to accomplish

the objectives of the Second National Heart Conference.

There will obviously be problems of financing and manpower for such a clinic. In the long run however the County may find that it is more economical to cure diseases in their early stages than to treat the far advanced complications. Unless we are prepared to take the action which is obviously needed, there is no point in having a National Heart Conference. The Hospital may say that this is impossible. A certain amount of reorientation in thinking concerning our health objectives is required. With adequate financial support the manpower problem could be solved.

We can dream of a regular annual examination of all citizens. It is obviously not possible at this time. We cannot expect the Supervisors to approach this objective. But at least a start could be made. We can ask the Supervisors to accept the concept that Preventive Medical Care is desirable for the health of the community. All I ask is that we make a start and in time the concept will grow.

If each of us returns to his community and asks the Supervisors and County Hospital—"Do we have a Well Man Clinic. If not, why not?" the Second National Heart Conference will have produced a significant advance in the control of Heart Disease, Cancer and Stroke.

## Quick Tracheotomy

IT WAS POINTED out to us that our article, Quick Tracheotomy [Oppenheimer, P., and Quinn, F. B., Jr.: Quick tracheotomy—incision at an easily identifiable, relatively safe site, *Calif. Med.*, 104: 51-53, January 1966] did not detail that coniotomy was only a temporary method of establishing an airway and in no way a substitute for a "classic" tracheotomy. I would like this made clear in your next issue as it seems to have confused a few people.

PETER OPPENHEIMER, M.D.



## WOMAN'S AUXILIARY

to the California Medical Association

### What Is WA-SAMA?

IN 1957, a handful of members of WA-AMA (Woman's Auxiliary to the American Medical Association), along with a few student wives and staff of SAMA (Student American Medical Association), formed WA-SAMA (Woman's Auxiliary to the Student American Medical Association), open for membership to wives of medical students, interns and residents. It was established with a two-fold purpose: (1) To prepare members for their future role as wives of physicians in the community where they will eventually live; (2) To bring wives and their families together with other medical families and medical groups for their mutual benefit.

The idea of WA-SAMA was very well received and today there are approximately 5,000 members in 53 chapters. Each year, more are joining. The national organization, WA-SAMA, is divided into seven regions, and is active on the local, regional and national level with meetings held at each level and programs designed for each of these categories.

WA-SAMA works closely with WA-AMA, the parent organization. A liaison officer is appointed by WA-AMA to WA-SAMA. She attends the WA-SAMA National Convention and offers assistance through the year. In many states, such as California, a state liaison officer is appointed to work with the local chapters. Since wives of interns and residents are not eligible for WA-AMA membership until their husbands enter practice, WA-SAMA offers them a "training ground" where they may prepare themselves for the role of a medical wife. We hope that eventually WA-SAMA members will become active WA-AMA and WA-CMA members when their husbands establish a practice.

There are many benefits to members; a few of them are:

- **NATIONAL HOUSING INFORMATION SERVICE** now operates in many cities from coast to coast. A WA-SAMA member planning to move to a new city obtains a standard form on which she indicates exactly what she wants in housing in the area to which she and her family are moving. She sends this to the housing chairman in that city who, in turn, returns the information to the applicant. Questions frequently

asked include rent, size, pets, furnished, distance to the hospital, shopping centers, churches, schools, etc. For those who have had experience in moving to a strange locale, this will be recognized as an excellent service.

- **PROGRAMS AND PROJECTS FILE** contains proven ideas and suggestions for programs, social activities, fund-raising, and service projects. At WA-SAMA conventions and regional meetings, local chapters have submitted their very best program and project ideas, and these have been compiled into a central file available to all local chapters.
- **INFORMATION-RELAY PROGRAM** has proven to be of great value to WA-SAMA wives who are leaving their local chapter. Each departing member fills out a standard form which is relayed via the Regional Vice-President either to the Interns and Residents Wives Group (in the case of a graduating medical student's wife) or to the Woman's Auxiliary to the American Medical Association (in the case of an intern's or resident's wife whose husband is entering private practice). The recipient of the Info-Relay Card will then be aware of the prospective member who is moving to that area and will welcome her into her group.
- **PUBLICATIONS**—*Chatterbox* and *The New Physician* communicate news from the national organization to each member periodically. *Chatterbox* is a newspaper edited by a staff of members from various chapters and is designed as an exchange of information among the chapters concerning their programs and activities combined with national news and reports. *The New Physician* is of a more general nature and is an effort to acquaint the future medical wife with the responsibilities, organizations, and problems of the medical profession.
- **NATIONAL LEGISLATIVE INFORMATION** gives up-to-date reports on current medical legislation before Congress. Future physicians' wives are well informed on current medical developments.

Dues are \$1 per year per member. The dues cover the cost of publishing *Chatterbox* and *The New Physician* and of sending national mailings. Subventions are given to the chapters in travel payments when they hold regional meetings.

WA-CMA sponsors six WA-SAMA chapters located at the California College of Medicine, U.C.L.A., U.S.C., Loma Linda at Loma Linda, Loma Linda at Los Angeles, and the San Diego Interns' and Residents' Wives. The Orange County General Hospital Interns' and Residents' Wives recently voted to become affiliated with WA-SAMA and the organization is in the process of petitioning for membership, which will bring the total to seven before the ninth annual National WA-SAMA Convention at the Statler-Hilton in Los Angeles on 11 to 15 May,



1966. On request, WA-CMA contributes an amount not to exceed \$200 to each chapter for one delegate to attend the National Convention. As experienced Auxiliary members, we try to be of assistance to the young wives in suggesting programs, service projects and benefits. In turn, these young women are an inspiration to us because their enthusiasm is contagious.

With all of our chapters in the vicinity of Los Angeles, the Woman's Auxiliary to the Los Angeles

County Medical Association appoints a Los Angeles area WA-SAMA chairman, who works closely with the state chairman, the WA-SAMA regional vice-president for Region 7 and the chapter presidents.

Hats off to the young energetic WA-SAMA working wives—supporting their husbands through medical schools—raising their young families—and paving the way to better medicine and a better world.

MRS. WARREN GOUX,

*State WA-SAMA Chairman*



# EDUCATION NOTICES

## Meetings and Courses

### COMMITTEE ON CONTINUING MEDICAL EDUCATION

THIS BULLETIN of the dates of continuing education programs and the meetings of various medical organizations in California is supplied by the Committee on Continuing Medical Education of the California Medical Association. In order that they may be listed here, please send communications relating to your future meetings or postgraduate courses to Committee on Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco, California 94102.

#### KEY TO ABBREVIATIONS AND SYMBOLS

Medical Centers and CMA Contacts  
for Postgraduate Course Information

<b>CMA:</b>	<b>California Medical Association</b> For information contact: Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco 94102. PROspect 6-9400, Ext. 68.
<b>LLU:</b>	<b>Loma Linda University</b> For information contact: W. F. Norwood, Ph.D., Associate Dean, Continuing Education, Loma Linda University School of Medicine, 1720 Brooklyn Ave., Los Angeles 90033, ANgeles 9-7241, Ext. 214.
<b>PRES. MED. CTR.</b>	<b>Presbyterian Medical Center</b> For information contact: Arthur Selzer, M.D., chairman, Education Committee, Presbyterian Medical Center, Clay and Webster Streets, San Francisco 94115, WEst 1-8000.
<b>UCLA:</b>	<b>University of California at Los Angeles</b> For information contact: Donald Brayton, M.D., Assistant Dean for Postgraduate Medical Education, 15-39 Rehabilitation Center, University of California Center for Health Sciences, Los Angeles 90024, 478-9711, Ext. 4345.
<b>UCSF:</b>	<b>University of California, San Francisco</b> For information contact: Seymour M. Farber, M.D., Dean, Educational Services and Director, Continuing Education, University of California Medical Center, Room 565-U, San Francisco 94122, 666-1692.
<b>USC:</b>	<b>University of Southern California</b> For information contact: Phil R. Manning, M.D., Associate Dean, Postgraduate Division, USC School of Medicine, 2025 Zonal Ave., Los Angeles 90033, Capital 5-1511, Ext. 300.
<b>STAN:</b>	<b>Stanford University</b> For information contact: Roy Cohn, M.D., Associate Dean for Graduate Affairs, Stanford University School of Medicine, 300 Pasteur Drive, Palo Alto, DAVenport 1-1200.

#### MARCH

March 19—**Catecholamines and Adrenergic Blocking Agents.** Sponsored by the American College of Cardiology and USC. Ambassador Hotel, Los Angeles. Saturday. Members: \$20., Non-Members: \$25. Contact: Executive Director, ACC, 9650 Rockville Pike, Washington, D.C. 20014.

March 19—**American College of Chest Physicians California Chapter Annual Meeting.** Biltmore Hotel, Los Angeles. Saturday. 9:00 a.m.-5:00 p.m. Contact: M. Rosenblatt, M.D., program chairman, County of Los Angeles Health Department, 220 North Broadway, Los Angeles 90012.

March 19—**Clinical Disorders of the Parietal Lobes.** UCSF. Saturday. 6¼ hours. \$20.

March 19—**Rheumatic Diseases: Diagnosis and Treatment.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

March 19-20—**California Radiological Society Annual Meeting.** Biltmore Hotel, Los Angeles. Saturday-Sunday. Contact: L. H. Garland, M.D., 450 Sutter Street, San Francisco.

March 20-23—**CALIFORNIA MEDICAL ASSOCIATION 95th Annual Session.** Scientific theme: "CURRENT CONCEPTS IN THERAPY: Coronary Artery Disease. Gastrointestinal Hemorrhage. Renal Failure." Biltmore Hotel, Los Angeles. Sunday-Wednesday. Contact: California Medical Association, 693 Sutter Street, San Francisco 94102.

March 21-April 11—**Medical Centers of Israel, Turkey, Greece and Italy.** Sponsored by USC. 18 hours. \$150.

March 25-27—**Postgraduate Assembly in Anesthesiology.** Sponsored by the Anesthesia Section, Los Angeles County Medical Association. International Hotel, Los Angeles. Friday-Sunday. 12 hours. \$25. Contact: Thomas W. McIntosh, M.D., secretary, Postgraduate Committee, 686 East Union Street, Pasadena.

March 26—**Endocrinology.** Pres. Med. Ctr. Saturday. 8 hours. \$30.

March 26-27—**Sex Problems in Clinical Practice: The Critical years.** UCSF. Saturday-Sunday. 12¾ hours. \$40.

March 28-April 1—**Mental Retardation Institute.** USC at Children's Hospital of Los Angeles. Monday-Friday. 35 hours. \$60.

March 29-30—**Southwestern Pediatric Society.** Statler Hilton Hotel, Los Angeles. Tuesday-Wednesday. Contact: Phillip Sturgeon, M.D., 1200 S. Vermont Avenue, Los Angeles 90006.

#### APRIL

April 1—**Fresno County Heart Association Annual Physicians Cardiovascular Symposium.** Hacienda Hotel, Fresno. Friday. \$15. Contact: Roger K. Larson, M.D., chairman, Professional Symposium Committee, FCHA, 1759 Fulton Street, Fresno.

April 1-2—**Contrast Media in Abdominal Disease: A Program for the Practicing Physician.** UCSF. Friday-Saturday. 11¾ hours. \$40.

April 1-2—**Annual Symposium on the Newborn.** Sponsored by the Pediatric Department, Southern California Permanente Medical Group, and Kaiser Foundation Hospitals. International Hotel, Los Angeles. Friday-Saturday. Contact: Shirley Gach, Room 3011, 4900 Sunset Blvd., Los Angeles 90027.



April 4-8—**Mental Retardation Institute.** USC. Monday-Friday.

April 5-8—**American Association of Anatomists.** San Francisco Hilton, San Francisco. Tuesday-Friday. Contact: Russell T. Woodburne, executive secretary, The University of Michigan East Medical Bldg., Ann Arbor, Michigan 48104.

April 6-20—**Practical Office Ophthalmology for the General Practitioner.** USC. Wednesdays. 6 hours.

April 6-May 11—**Psychiatry in General Practice.** UCSF at Stockton State Hospital, Stockton. Wednesdays. 12 hours. \$10.

April 7-June 9—**Ward Walks in Rare Diseases.** USC at Los Angeles County Hospital. Thursday evenings. 18 hours. \$100.

April 13-15—**The Pacific Regional National Rehabilitation Association Conference.** Sheraton-Palace Hotel, San Francisco. Wednesday-Friday. \$12., including keynote luncheon. Contact: Tak Taketa, chairman, Publicity Committee, 1111 Jackson Street, Rm. 5040, Oakland 94607.

April 13-16—**American Orthopsychiatric Association.** San Francisco Hilton, San Francisco. Wednesday-Saturday. Contact: Marion F. Langer, Ph.D., executive secretary, 1790 Broadway, New York 10019.

April 14-16—**Retinal Detachment Conference.** Lions Eye Bank. Thursday-Saturday. 8 hours. \$100. Contact: Eva del Oro, secretary, Lions Eye Bank, 2018 Webster Street, San Francisco.

April 16—**Ankle Injuries in Athletics.** UCLA. Saturday. 6 hours. \$25.

April 16-17—**The Uncertain Quest: The Teen-Ager's World.** UCSF. Saturday-Sunday. 12¾ hours. \$15.

April 19-May 24—**San Francisco Academy of General Practice Postgraduate Medical and Surgical Clinics.** French Hospital, San Francisco. Tuesdays. \$20 members, \$25 non-members. Contact: Rafael P. Bricca, M.D., 909 Hyde Street, San Francisco.

April 22-23—**Pediatrics and Pediatric Surgical Presentations.** Amphitheater Conference Room, Children's Hospital of Orange County, 1109 West La Veta, Orange 92666. Friday-Saturday. Contact: Merl J. Carson, M.D., Medical Director, CHOC.

April 23-24—**Mental Retardation and Emotional Disturbance in Childhood and Adolescence.** UCSF at Sutter Memorial Hospital, Sacramento. Saturday-Sunday. 9½ hours. \$7.

April 25-27—**Annual Meeting of the Council on Medical Television.** UCSF. Monday-Wednesday. 20 hours. \$15 members, \$20 non-members.

April 28-29—**General Surgery.** UCSF. Thursday-Friday. 12½ hours. \$60.

April 28-30—**REDWOOD REGIONAL CONFERENCE** presented by California Medical Association in cooperation with USC. Konocti Harbor Inn, Clear Lake. Thursday noon-Saturday noon. \$15. "Cardiovascular Disease, Endocrinology, Office Techniques in Patient Interviews." Chairman: Lucius L. Button, M.D., 1102 Montgomery Drive, Santa Rosa.

April 30—**Recent Advances in Infant Cardiology.** USC at Children's Hospital of Los Angeles. Saturday. 7 hours.

April 30-May 1—**Clinical Considerations in Mental Retardation.** UCSF at Sonoma State Hospital, Eldridge. Saturday-Sunday. 10¾ hours. \$10.

## MAY

May 1-5—**American Society for Microbiology.** Biltmore Statler Hilton Hotel, Los Angeles. Sunday-Thursday. Contact: R. W. Sarber, executive secretary, 115 Huron View Blvd., Ann Arbor, Michigan.

May 3-6—**American College Health Association.** El Cortez Hotel, San Diego. Tuesday-Friday. Contact: Benjamin R. Reiter, M.D., executive director, University of Miami, Bldg. 37-X, 1200 Dickinson Drive, Coral Gables, Florida 33146.

May 5-7—**Ear, Nose, Throat.** UCSF. Thursday-Saturday. 18 hours. \$50.

May 5-26—**Neuropsychiatric Management in Daily Practice.** UCSF at Modesto State Hospital, Modesto. Thursdays. 8 hours. \$7.

May 6—**Symposium on Hypertension.** USC at Statler Hilton Hotel, Los Angeles. Friday. 7 hours.

May 6-7—**Congenital and Hereditary Defects of the Musculoskeletal System.** UCSF. Friday-Saturday. 12 hours. \$40.

May 7—**Ventura County General Hospital Annual Staff Seminar.** VCGH. Saturday. 6 hours. No fee. Contact: G. K. Ridge, M.D., VCGH, 291 Loma Vista Road, Ventura.

May 7-8—**Dynamic Measurements with Radioisotope Techniques for Evaluating Organ Function and Circulation.** UCLA. Saturday-Sunday.

May 7-8—**Seminar on Chronic Respiratory Problems.** Lebanon Hall, Cedars of Lebanon Hospital, 4833 Fountain Avenue, Los Angeles. Saturday-Sunday. 12 hours. \$15. Contact: Mr. Seymour P. Stein, seminar coordinator, Ben R. Meyer Rehabilitation Center, CLH.

May 11—**American Cancer Society Scientific Session.** St. Francis Hotel, San Francisco. Wednesday. Contact: Lewis W. Guiss, M.D., 1930 Wilshire Blvd., Los Angeles 90057.

May 12-15—**Hawaii Medical Association Annual Meeting.** Arthritis and Psychiatry. Princess Kaiulani Hotel, Honolulu. Thursday-Sunday. 15 hours. \$35. Contact: Miss Lee McCaslin, executive secretary, 510 S. Bere-tania, Honolulu, Hawaii 96813.

May 13-14—**SAN JOAQUIN VALLEY COUNTIES—Regional Postgraduate Institute presented by California Medical Association in cooperation with UCLA.** Ahwahnee Hotel, Yosemite. Friday-Saturday. \$15. "Cerebral and other Peripheral Vascular Disease, Headache." Chairman: Dale Kirkegaard, M.D., 2432 Calaveras Street, Fresno.

May 14—**Humboldt-Del Norte Medical Society Annual Medical Symposium: "Frontiers in Medicine."** Eureka Inn, Eureka. Saturday. 4 hours. Contact: Stanwood S. Schmidt, M.D., president, 707 K Street, Eureka.

May 14-15—**Hypnosis, A Critical Evaluation.** UCSF at Napa State Hospital, Imola. Saturday-Sunday. 12 hours. \$10.

May 18—**Peripheral Vascular Disease.** USC. Wednesday. 7 hours.

May 19—**California Heart Association Annual Scientific Session.** Ambassador Hotel, Los Angeles. Thursday. 6 hours. No fee. Contact: Arthur Feinfeld, M.D., CHA, 1370 Mission Street, San Francisco.

May 20-21—**San Diego Academy of General Practice Annual Postgraduate Symposium presented in cooperation with University of Oregon School of Medicine.** Vacation Village Hotel, Mission Bay, San Diego. Friday-Saturday. Contact: Orlando P. Johann, M.D. 731 E. Broadway, El Cajon.

May 20-21—**Pain.** UCSF. Friday-Saturday. \$40.

May 20-22—**Complications in Modern Medical Practice.** UCLA. Friday-Sunday. 18 hours.

May 21—"Clinic Day"—**Diseases of Medical Progress.** Channing House Auditorium, Palo Alto. Saturday. 9:00 a.m. to 3:30 p.m. Contact: R. Hewlett Lee, M.D., Palo Alto Medical Clinic, 300 Homer, Palo Alto.

May 23-25—**American Thoracic Society Annual Meeting.** Hilton Hotel, San Francisco. Monday-Wednesday. Contact: James Kieran, M.D., chairman, Medical Sessions Committee, American Thoracic Society, 1790 Broadway, New York, N.Y. 10019.

May 28-June 29—**Medical Centers of Europe.** USC. 50 hours. \$250.

May 20-21—**San Diego Academy of General Practice Annual Postgraduate Symposium** in cooperation with University of Oregon School of Medicine. Vacation Village Hotel, Mission Bay, San Diego. Friday-Saturday. Contact: Orlando P. Johann, M.D., 731 E. Broadway, El Cajon.

## JUNE

June 4-5—**The Cervical Spine.** UCSF. Saturday-Sunday.

June 10-11—**Convulsive Disorders.** UCSF. Friday-Saturday.

June 11-12—**The Drug Takers.** UCLA. Saturday-Sunday. 12 hours.

June 16-19—**California Society of Anesthesiologists Biennial Scientific Meeting.** Sahara Tahoe Hotel, South Shore, Lake Tahoe. Thursday-Sunday. \$25. Contact: Mr. Norman R. Catron, executive secretary, CSA, 39 North San Mateo Drive, San Mateo 94401.

June 17—**Attending Staff Association of Olive View Hospital Symposium on Infectious Diseases.** OVH, Olive View. Friday. Contact: Joseph K. Indenbaum, M.D., secretary-treasurer, ASAOVH, Olive View.

June 18—**Diagnosis and Management of Infectious Diseases.** Amphitheater Conference Room, Children's Hospital of Orange County, 1109 W. La Veta, Orange

92666. Saturday. 8:30 a.m. to 4:00 p.m. \$5 (lunch included). Contact: Merl J. Carson, M.D., Medical Director, CHOC.

June 22-24—**Highlights of Modern Ophthalmology.** Lions Eye Bank. Wednesday-Friday. 8 hours daily. \$75. Contact: Eva del Oro, secretary, Lions Eye Bank, 2018 Webster Street, San Francisco.

June 22-24—**Treatment of Fractures.** USC. Wednesday-Friday.

June 23-25—**SACRAMENTO VALLEY COUNTIES—Regional Postgraduate Institute** presented by California Medical Association in cooperation with Stanford. Harvey's Resort Hotel, Lake Tahoe. Thursday noon-Saturday noon. \$15. "Advances in Therapy: Diseases of Medical Progress, Newer Antibiotics, Peptic Ulcer Disease, Cosmetic Plastic Surgery." Chairman: John N. Miller, Jr., M.D., 5301 F Street, Sacramento.

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# The Physician's BOOKSHELF



**YEAR BOOK OF ANESTHESIA** (1965-1966 Year Book Series)—Edited by Stuart C. Cullen, M.D., Professor and Chairman, Department of Anesthesia, University of California Medical Center, San Francisco, Year Book Medical Publishers, Incorporated, 35 East Wacker Drive, Chicago, Ill., 1965. 389 pages, \$8.50.

This volume contains excellent abstracts of original articles published between September 1964 and 1965. The designation "(1965-1966 Year Book Series)" is somewhat misleading. As with Yearbooks for other medical specialties, the objective is to provide the anesthesiologist with a means for reviewing the related medical literature published during the past year. Since anesthesiology is concerned with so many disciplines in basic sciences and clinical specialties, study by a practicing physician of all pertinent original articles in numerous diverse publications is not reasonable. In this volume, abstracts are grouped by subject with sections on non-volatile depressant drugs, inhalation agents and technics, relaxants, regional anesthesia, and sections on subspecialties in anesthesiology. In addition there are sections on circulation (with seven subsections), respiration, complications, hyperoxia, hypothermia, clinical problems and inhalation therapy. This arrangement, plus the indices by both subject and author, make the volume valuable for review of a special subject.

Abstracts are concise but contain information concerning both investigative methods and results and are followed by practical comments by Dr. Cullen, an experienced author, editor and teacher. In some abstracts, essential data are reproduced in graphs and tables.

The convenient size of the volume makes it easily portable and available for reading of several short abstracts at odd moments which otherwise might not be used to advantage.

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**NEUROLOGICAL SURGERY OF TRAUMA**—Prepared and published under the direction of Lieutenant General Leonard D. Heaton, The Surgeon General, United States Army. Editor in Chief: Colonel John Boyd Coates, Jr., MC, USA; Editor: Arnold M. Meierowsky, M.D., Office of The Surgeon General, Department of the Army, Washington, D.C., 1965. 604 pages, 273 illustrations, 35 tables, available for purchase at \$6.25 per copy from the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402.

This beautifully prepared multi-authored work is timely and likely to be enduring since it reflects in a single volume the major neurosurgical experience of United States forces in the Korean war. Its perspective is not narrowly limited to this period in our history for it brings the follow-up analyses of neurosurgical casualties into meaningful focus for future guidance of those who will treat trauma to the nervous system. The lessons of the two great World Wars have been reassessed in the light of the Korean experience, and the personal involvement of many of the authors and especially the editor makes this work compelling in the experiences which it surveys. This is an operating surgeon's reference work. The individual surgical problems are treated pedantically and with precision; the pattern of treatment in each case is based upon

case analyses and statistical surveys of results. The value of the Korean case-load study is revealed in the presentation of detailed management protocols. Concepts relative to the handling of traumatic abscess, retained metallic fragments, through and through penetrating missile wounds, wounds involving the accessory nasal sinuses, etc., are shown to be modified as compared with older practices and the new experience is sufficiently broad to insist that every surgeon review his tenets relating to such injuries.

The illustrations of operating technique are simple and clear, and will appeal equally to the general surgeon who is not specifically trained in neurological surgery but who does and will continue to carry much of the load of disaster trauma.

Some variation in quality in the chapters is unavoidable and the inclusion of the management of herniating disc disease deviates somewhat from the otherwise quite immediate relevance of the chapters to military surgery. Yet trauma is not limited to warfare, and the civilian surgeon should make the contents of this volume part of his knowledge. Little new is found in the chapters on cranioplasty or peripheral nerve injuries and one might comment upon the meager mention of newer contributions in the management of, for example, the skeletal aspects of spine injuries, dural grafting, and nerve grafting. These omissions do not detract for the time base of the Korean War explains the lack of inclusion of more recent and unproven techniques.

Each chapter concludes with its own references. The index is quite complete and, for the very modest price, every surgeon in civilian or military practice who sees and cares for the injured patient should read and possess this work. It is mandatory reading for all neurosurgeons. It belongs in every medical library and it will be of historical interest as a sequel to the military history of *Neurosurgery in World War II*.

WALTER EUGENE STERN, M.D.

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**GIVE AND TAKE**—The Biology of Tissue Transplantation—Francis D. Moore, M.D. Anchor Books—Doubleday & Company, Inc., Garden City, New York, 1965. 216 pages, \$1.25 (Paperback). (Hardbound: W. B. Saunders Company, Philadelphia, 1964—182 pages, \$5.50.)

One of the major problems of modern society is to make the language and interests of science comprehensible to the larger but equally concerned nonscientific community. Indeed, as science becomes more complex, it becomes involved in social and moral issues which can only be resolved if one understands both science and society. This delightful book, entitled *Give and Take*, is an exciting account of the biology of tissue transplantation, written by Francis D. Moore, Surgeon-in-Chief of the Peter Bent Brigham Hospital in Boston, and Moseley Professor of Surgery at Harvard Medical School. Dr. Moore has a particular flair for the lucid, dramatic and sparkling interpretation of science to the lay audience.

The book deals with the problems of transplanting live tissue from one individual to another. The first individual



gives the live tissue. It must take and live permanently on the second individual if it is to be of value in solving his biologic needs. The rejection of the tissue of one individual by another is the basis of our individuality and specificity, and is an unsolved problem in biology. The cause of the rejection is a difference in chemical or antigenic structure between the two individuals. This difference can be altered, attenuated, and, hopefully, breached if immunity between individuals could be suppressed or tolerance between individuals induced. Current immunological theories suggest that tolerance can be induced if the genetic disparity between individuals is not large, and if the immune reactions between individuals can be suppressed. This book makes a particular effort to clarify the basic scientific terms at play, and to illustrate the origins of our knowledge concerning these basic scientific phenomena with anecdotes, line drawings, simplicity and clarity of writing, and lucidity of expression. Into this scientific fabric is woven the charm of a gifted storyteller, and the book truly is an exciting story for both doctors and laymen as to the methods whereby the most advanced and scientific knowledge is carried over into the clinical care of patients. This type of communication and translation will be of increasing importance to science and society in the years ahead. This is one of the first areas in which practical medical therapy is contingent upon a universal understanding of basic biological phenomena, and Dr. Moore has done an outstanding job in portraying in a vivid and exciting manner the interplay between the acquisition of knowledge, its understanding, its utilization, and its inter-relationships to moral and ethical considerations in the cure of desperate diseases.

Dr. Moore is to be congratulated on an excellent achievement in scientific writing.

VICTOR RICHARDS, M.D.

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**MANAGEMENT OF JUVENILE DIABETES MELLITUS**—Howard S. Traisman, M.D., Assistant Professor of Pediatrics, Northwestern University Medical School; Associate Attending Physician and Head of the Diabetes Clinic, Children's Memorial Hospital, Chicago, Illinois; and Attending Physician, Evanston Hospital Association, Evanston, Illinois; and Alvah L. Newcomb, M.D., Associate Professor of Pediatrics, Northwestern University Medical School; Associate Attending Physician, Children's Memorial Hospital, Chicago, Illinois; and Attending Physician, Evanston Hospital Association, Evanston, Illinois. The C. V. Mosby Company, St. Louis, 1965. 147 pages, \$12.75.

The authors state in the preface to this book that it is their purpose to provide for the pediatrician and general practitioner who is infrequently called upon to treat or diagnose diabetes a concise and practical method of management for the juvenile diabetic. This book is most valuable in those sections which describe the procedures and methods of management used by the authors in their own hospitals. The physician who is inexperienced in the treatment of diabetes and who does not have sufficient time to consult one of the current standard texts in diabetes may find this information useful and in a readily accessible form.

This is not a textbook or reference work and the authors have made a number of short statements about our basic knowledge and about the nature of diabetes and its complications which are unnecessarily brief and incomplete. In a number of instances their statements would be challenged by experts in the field and this book will have little interest for the specialist or the physician experienced in the treatment of diabetes mellitus.

JERALD C. NELSON, M.D.

**OBSTETRICS—Thirteenth Edition**—(From the Original Text of Joseph B. De Lee, M.D.)—J. P. Greenhill, M.D., F.A.C.S., F.I.C.S. (Hon.), F.A.C.O.G., Senior Attending Obstetrician and Gynecologist, The Michael Reese Hospital; Obstetrician and Gynecologist, Associate Staff, The Chicago Lying-in Hospital; Attending Gynecologist, Cook County Hospital; Professor of Gynecology, Cook County Graduate School of Medicine. W. B. Saunders Company, Philadelphia, Pa., 1965. 1246 pages, \$20.00.

A reviewer writing for another journal has referred to this edition of Greenhill's "Obstetrics" as practically a new book and suggests that it has attained a pinnacle reached by few textbooks. Though this volume certainly retains a spot in the list of top ranking American obstetric productions, one is inclined to question both of these claims. In the first place there is no real change in the general format of the book and relatively little in the topical material covered. Additional contributors have supplied chapters (both replacements for previous offerings and also some new subjects) concerning their areas of special competence. Thirty-four names of contributing authors are listed now as against twenty-three in the last edition. (In the preface Greenhill says only 32 others participated, but this appears to have been an erroneous count. The name of one contributor appears only as a footnote on page 725, thus it seems that at least 35 were involved.) On the title page one reads that there are 1,193 figures, but the last figure in the book is numbered 1,106. Some 87 figures and at least a few contributors got lost somewhere in the Saunders pressroom. But these losses have been counterbalanced by adding, unfortunately for the medical student, nearly 150 pages to the length of the book.

Notwithstanding these arithmetic difficulties, it is obvious—as I pointed out in reviewing the twelfth edition five years ago—that many parts of this textbook merit the attention of all students and practitioners of obstetrics. The two new opening chapters by Bent Boving (reproductive anatomy) and Elizabeth Ramsey (placenta) are superb and warrant careful study by teachers as well as their trainees. Caldeyro-Barcia has described uterine activity in labor, Fluhmann has recapitulated his studies on cervical morphology, Hon discusses fetal electrocardiography, Daniel Moore describes obstetric anesthesia in considerable detail, and so on through the long list of experts and a wide array of topics.

Two new chapters are devoted to genetics, the first touching on problems in counseling (fashioned from Sheldon Reed's monograph), while the second is a particularly authentic piece by Murray Barr on cytogenetics and chromosomal abnormalities. A short essay on contraception has replaced Schmitz's interesting section on medicomoral problems, an exchange difficult to explain, and the traditional chapter on mutilating obstetric operations on the dead fetus has been dropped entirely for obvious reasons.

Except for insertion of the chapters by new contributors, there appears to have been rather minimal revision of the rest of the text. In at least a few areas the new material might have been somewhat better integrated into the existing sections. For example, the previous edition contained three sequential chapters dealing with the clinical course of labor, the passages, and finally the passengers. Currently, Caldeyro's views on uterine contractions have been blown up from two to 26 pages and slipped in as a separate chapter between the "clinical course" and the "passages" to make a cumbersome section which could have been improved by vigorous editing. Some of the reference lists suffer from lack of up-dating. Indeed, in certain instances the older lists appear to have been cropped a bit by the printer when the bottom of a page was



reached; at the end of the final chapter, for instance, two rather modern references have vanished and one lone-some item dated 1934 remains.

Improvements in typography, particularly for the section, chapter, and paragraph headings, are quite apparent and add much to the general attractiveness of the volume, and the index is admirable in its detail. Despite its minor imperfections, until such time as its serious competitors appear in new editions there is no doubt that Greenhill's book will be at the top of the best seller list in the American obstetric field.

C. E. McLENNAN, M.D.

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**PRINCIPLES OF CHEST ROENTGENOLOGY—A Programmed Text**—Benjamin Felson, M.D., Aaron S. Weinstein, M.D., and Harold E. Spitz, M.D., Department of Radiology, University of Cincinnati College of Medicine, Cincinnati, Ohio. W. B. Saunders Company, Philadelphia, 1965. 221 pages, \$6.00 (Paperback).

This is a most enjoyable, interesting book that is both instructive and accurate. The illustrations are of excellent quality and the questions are for the most part very well phrased.

There is a wealth of material and the reader with some preliminary skills can benefit considerably from going through this programed text and answering the questions.

The only criticism that one might have with this book is a slight over-emphasis on certain signs such as the silhouette sign and the air bronchogram sign, but this may be a matter of personal philosophy of the authors and may be justifiable. The general anatomic approach, with the first chapter devoted to techniques of examination, is most laudable. The last chapter, presenting material on the many causes of rib notching, is offered by the authors as a bonus and admittedly doesn't quite mesh with the rest of the subject matter.

In summary, there are very few books available that make learning pure, unadulterated fun. This is one of them.

ALEXANDER R. MARGULIS, M.D.

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**REFRACTION—A Programmed Text**—Robert D. Reinicke, M.D., Howe Laboratory of Ophthalmology, Harvard Medical School, Massachusetts Eye and Ear Infirmary; and Robert J. Herm, M.D., Harvard Medical School, Massachusetts Eye and Ear Infirmary. With a foreword by Albert E. Sloane, M.D. This book also includes a booklet—Panel Text, and a Stereo Viewer. Appleton-Century-Crofts (Division of Meredith Publishing Company), New York, N.Y., 1965. 336 pages, \$12.50 (Paperbound).

This textbook on refraction is a refreshingly new approach to resident teaching which is long overdue. As far as I know, programing material in ophthalmology has not been tried before and I hope that more ophthalmological material will be put in program form for easier and more interesting reading.

This text includes chapters on:

(1) Neutralization of Lenses and the Measurement of Visual Acuity, (2) Accommodation, (3) Cycloplegics, (4) Myopia, Hyperopia, and Astigmatism, (5) Interpupillary Distance and Trial Frame, (6) Retinoscopy, (7) Subjective Methods of Verifying Retinoscopy, (8) Heterophorias, (9) Prescription of Glasses, (10) Bifocals, (11) Spectacle Aberrations.

There are accompanying gadgets for stereo-observations.

This book is recommended for review of refraction and for the first year resident in ophthalmology.

ROBERT M. SINSKEY, M.D.

**RYPINS' MEDICAL LICENSURE EXAMINATIONS—Topical Summaries and Questions—Tenth Edition**—Arthur W. Wright, M.D., Professor of Pathology, Albany Medical College of Union University; Senior Pathologist, Albany Medical Center Hospital; formerly Secretary, New York State Board of Medical Examiners; with the collaboration of a Review Panel. J. B. Lippincott Company, Philadelphia, Pa., 1965. 849 pages, \$12.50.

This book, now in its tenth edition, continues to hold its place as a valuable text for students preparing for medical licensure examinations. It is divided into two sections, Basic Medical Sciences and Clinical Sciences. Separate reviews of each subject followed by questions related to the chapter are presented.

Practical application of physiology and biochemistry in many therapeutic procedures today requires a good understanding of these two basic sciences in particular.

Most helpful to the student are the pages on body fluids, the kidneys, circulation and the respiratory system appearing in the chapter on physiology as well as the discussion of the chief materials of living matter, enzymes, and the metabolism in the chapter on biochemistry.

The chapter on surgery is remarkable in the clear, concise manner in which it covers the diagnosis and treatment of nearly all surgical conditions. The chapter on internal medicine as likewise brief and to the point avoiding length and repetition by omitting certain topics when possible that have been taken up in the other chapters. For example, vitamin deficiencies are discussed in the chapter on biochemistry and many infections are adequately dealt with under microbiology. Much could be written on such topics as Addison's disease or Diabetes Mellitus but the author confines himself to the essentials of diagnosis and practical management in an excellent manner.

In the remaining chapters on Gynecology and Obstetrics, Public Health and Psychiatry the same adherence to clearness and conciseness prevails without sacrificing up-to-date knowledge.

After reviewing the text, therefore, its value both as a review and reference book for the practicing physician and for the students preparing for examinations cannot be denied.

HENRY GIBBONS III, M.D.

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**COLOUR VISION, Physiology and Experimental Psychology—Ciba Foundation Symposium**—Edited by A. V. S. de Reuck, M.Sc., D.I.C., A.R.C.S. and Julie Knight, B.A. Little, Brown and Company, Boston, 1965. 382 pages, \$12.50.

This collection of papers by the outstanding scholars in the field of color vision is interesting even to the clinical ophthalmologist. The papers are presented under the following categories:

Visual Pigments  
Duplidity theory and the microstructure of the retina  
Theories of Color Vision  
Human Color Vision  
Animal Color Vision

The discussions are lively in some instances.

The paper by Dr. Land on "The retinex" is particularly noteworthy and attracted a good deal of attention at the meeting. Apparently Dr. Land is not only a first rate businessman (Polaroid Land Camera), but excels as a physiological theoretician.

This book is recommended as a reference text and for those ophthalmologists who are particularly interested in color vision.

R. M. SINSKY, M.D.



**FLUID AND ELECTROLYTES IN NEUROLOGICAL SURGERY**—Burton L. Wise, A.B., M.D., Associate Professor of Neurological Surgery, University of California School of Medicine, San Francisco; Attending Neurological Surgeon, Fort Miley Veterans Administration Hospital, and San Francisco General Hospital; Consultant in Neurological Surgery, Letterman General Hospital, San Francisco, Calif. Charles C Thomas, Publisher, Springfield, Ill., 1965. 117 pages, \$6.00.

In this uncomplicated and lucidly written little monograph the author presents his analysis of several years' experience in the management of the fluid and electrolyte balances in neurosurgical patients. By adapting his balance studies to patterns which have proved helpful in the hands of others, Dr. Wise perpetuates a continuity in presentation of data which avoids the confusing morass of detail which often detracts from the ease of comprehension of similar fluid and electrolyte studies.

The usual metabolic response of the neurosurgically-treated patient is similar in respect of water and electrolytes and nitrogen changes to that found in other patients responding to trauma. The author recommends the use of body weight determination and fluid intake and output measurement as the basic mensuration of importance in guiding analysis of patient care. His metabolic analyses of patients suffering from head injury, undergoing specific stressful neurological diagnostic studies, or suffering from hypophyseal disease lead him to practical conclusions in recommending management.

The important syndromes of hypersomolality and hypo-osmolality are treated and the pathogenesis is described whereby the primary neurological disease may contribute to the development of either of these alterations. There is a clear discourse on how these altered fluid states in themselves can influence the clinical neurological picture and complicate its analysis.

Where specific central nervous system lesions may alter fluid and electrolyte input, these are individually described. In each major section there are presented representative case histories, balance data, a summary of the experience of other workers in the field, and the author's own recapitulation and recommended protocol of management.

The book is punctuated with easily deciphered charts, the bibliography is reasonably chosen, and the index is complete. This is recommended reading for all neurosurgeons and neurologists and their trainees, as well as anesthesiologists and other physicians who manage the day to day care of patients suffering from central nervous system trauma or disease.

WALTER EUGENE STERN, M.D.

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**BONE TUMORS**—Louis Lichtenstein, M.D., Clinical Professor of Pathology, University of California, San Francisco; Professor Extraordinario, National University of Mexico; Honorary Member, Spanish Orthopedic Society (SECOT); Honorary Member, Western Orthopedic Association; Fellow, New York Academy of Medicine; Consultant in Pathology, Los Angeles County Hospital. The C. V. Mosby Company, St. Louis, 1965. 411 pages, \$16.75.

Lichtenstein's third edition of "Bone Tumors" enlarges on his previous texts of 1952 and 1959. A number of chapters have been largely rewritten. Many new roentgenographic and photomicrographic illustrations have been added or have replaced old less adequate illustrations. The references for each chapter have been enlarged. The appendices deal with non-neoplastic lesions which may be mistaken for tumor as well as tumors of joints, bursa and tendon sheath.

A new chapter on benign and malignant chondroid tumors has been added. This is based on Lichtenstein's publication in "Cancer" 1959 of 25 unusual and largely unfamiliar chondroid tumors. Since then he has seen 30 additional cases that fall in this classification. The majority of these lesions were atypical benign chondroblastoma or atypical chondromyxoid fibromas. Only the multicentric lesions were shown to be obviously malignant. The cytological patterns are discussed in detail, but the roentgen findings are nonspecific. These tumors are rare and difficult to classify, but with this as a guide it can be expected that our knowledge of their behaviour will be expanded in the future.

Lichtenstein has expanded the chapter on benign osteoblastoma in which he is particularly interested, and this is an excellent radiologic and microscopic study with differential diagnosis. The newer concepts of nonosteogenic fibroma are presented in a chapter with discussion of its relationship to metaphyseal fibrous defects.

It is to be noted that the differential diagnosis of bone tumors is incompletely discussed from the roentgen standpoint in many of the chapters, although the histopathology is thoroughly covered. There is incomplete discussion of paraosteal sarcomas and aneurysmal bone cysts from the roentgenological aspect, and although the latter is not considered tumor, accurate diagnosis is essential for therapy and it must be differentiated from the more aggressive lesions.

I would disagree with his statement "An unverified roentgen diagnosis of vertebral hemangioma may not be too trustworthy." Certainly there are some atypical lesions, but the majority are easily recognized by the radiologist and need no biopsy.

For intelligent treatment an accurate diagnosis is needed. Often this can be made by the roentgenologist, but pathological confirmation in most cases is desirable, and this volume reflects the author's vast experience and ability. To quote "The positive identification from biopsy specimens may be difficult if the area shows extensive deterioration, necrosis and secondary leucocyte reaction." This volume should do much to improve and expand the pathologist's role in bone tumor diagnosis. It must be remembered however that needle biopsy may not represent the lesion as a whole and may in fact be misleading, so slide interpretation alone is not adequate for diagnosis, but the history, roentgenograms and the surgeon's findings should also be evaluated.

The clinical material is all from Lichtenstein's files and his recommendations regarding therapy are sound. This is a valuable book for pathologists, radiologists and orthopedic surgeons.

M. E. MOTTRAM, M.D.

\* \* \*

**A CURRENT TECHNIQUE OF AORTOILIAC AND FEMOROPLOPITAL ENDARTERECTOMY FOR OB-LITERATIVE ATHEROSCLEROSIS**—Jack A. Cannon, M.D., Department of Surgery, School of Medicine, University of California, Center for Health Sciences, Los Angeles, California. Charles C Thomas, Publisher, Springfield, Ill., 1965. 54 pages, \$4.75.

This is an excellent and concise discussion of some challenging clinical problems. The illustrations are numerous and clear. The text is easy to read and witty. The fledgling surgeon is invited to improve the described techniques which have made the author pre-eminent in his field. The monograph is highly recommended for practicing surgeons and house officers alike.



# BOOKS RECEIVED

*Books received by CALIFORNIA MEDICINE are acknowledged in this column. Selections will be made for more extensive review in the interest of readers at space permits.*

**BASIC GASTRO-ENTEROLOGY**—Including Diseases of the Liver—J. M. Naish, M.D., F.R.C.P., Consultant Physician, Frenchay Hospital, Bristol; Lecturer in Medicine, University of Bristol; and A. E. A. Read, M.D., F.R.C.P., Reader in Medicine, University of Bristol; Honorary Assistant Physician, Bristol Royal Infirmary, United Bristol Hospitals, and South-Western Regional Hospital Board. With chapters by T. J. Butler, M.D., F.R.C.S., and K. T. Evans, M.R.C.P., F.F.R. Distributed in the United States by the Williams & Wilkins Company, Baltimore 2, Maryland, 1965. 351 pages, \$11.00.

**THE AMERICAN HEALTH SCANDAL**—Roul Tunley. Harper & Row, Publishers, New York, N.Y., 1966. 282 pages, \$4.95.

**THE CELL—Its Organelles and Inclusions—An Atlas of Fine Structure**—Don W. Fawcett, M.D., Hersey Professor of Anatomy, Harvard Medical School. W. B. Saunders Company, Philadelphia, 1966. 448 pages, \$11.00.

**CIBA FOUNDATION STUDY GROUP NO. 22: GONADOTROPINS: PHYSICO-CHEMICAL AND IMMUNOLOGICAL PROPERTIES**—In Honour of Dr. C. Hamburger—Edited by G. E. W. Wolstenholme, O.B.E., F.R.C.P., F.I. Biol., and Julie Knight, B.A. Little, Brown and Company, Boston, 1965. 125 pages, 28 illustrations, \$3.50.

**CONTROVERSY IN INTERNAL MEDICINE**—Edited by Franz J. Ingelfinger, M.D., Conrad Wesselhoef Professor of Medicine, Boston University School of Medicine; Arnold S. Relman, M.D., Professor of Medicine, Boston University School of Medicine; and Maxwell Finland, M.D., George Richards Minot Professor of Medicine, Harvard Medical School. W. B. Saunders Company, Philadelphia, 1966. 679 pages, \$14.50.

**CURRENT PEDIATRIC THERAPY—1966-1967**—Sydney S. Gellis, M.D., Professor and Chairman, Department of Pediatrics, Tufts University School of Medicine; Pediatrician-in-Chief, Boston Floating Hospital for Infants and Children, Tufts-New England Medical Center, Boston; and Benjamin M. Kagan, M.D., Director, Department of Pediatrics, Cedars of Lebanon Hospital, Division of Cedars-Sinai Medical Center; Professor of Pediatrics, University of California at Los Angeles. W. B. Saunders Company, Philadelphia, Pa., 1966. 956 pages, \$17.50.

**FERMENT IN MEDICINE—A Study of the Essence of Medical Practice and of Its New Dilemmas**—Richard M. Magraw, M.D., Professor, Departments of Internal Medicine and Psychiatry, University of Minnesota; Director, Comprehensive Clinic Program, University of Minnesota Medical School. With a chapter on Automation in Medicine written in collaboration with Daniel B. Magraw, M.B.A., Lecturer in Accounting, School of Business Administration, and Lecturer in Public Administration, School of Public Administration, University of Minnesota. W. B. Saunders Company, Philadelphia, 1966. 272 pages, \$6.50.

**FUNDAMENTALS OF CLINICAL HEMATOLOGY—Second Edition**—Byrd S. Leavell, M.D., Professor of Internal Medicine; Physician-in-Charge, Hematology Section, School of Medicine, University of Virginia; Attending Physician, University of Virginia Hospital; and Oscar A. Thorup, Jr., M.D., Associate Professor of Internal Medicine; Physician-in-Charge, Hematology Clinic, School of Medicine, University of Virginia; Attending Physician, University of Virginia Hospital. W. B. Saunders Company, Philadelphia, 1966. 597 pages, \$12.50.

**THE HEART—Its Function in Health and Disease**—Arthur Selzer, M.D. University of California Press, Berkeley and Los Angeles, 1966. 301 pages, \$5.95.

**INJURIES OF NERVES AND THEIR CONSEQUENCES (Vol. II IN AMERICAN ACADEMY OF NEUROLOGY REPRINT SERIES ISSUED BY DOVER)**—S. Weir Mitchell, M.D. With a new Introduction by Lawrence C. McHenry, Jr. Dover Publications, Inc., New York, 1965. 377 pages, \$2.75 (Paperback).

**MAN AND AFRICA**—Ciba Foundation Symposium—Jointly with The Haile Selassie I Prize Trust under the patronage of His Imperial Majesty Haile Selassie I, Emperor of Ethiopia—Edited by Gordon Wolstenholme and Maevae O'Connor. Little, Brown and Company, Boston, 1965. 400 pages, 21 illustrations, \$7.50.

**PEDIATRIC THERAPY—Second Edition**—Harry C. Shirkey, B.S. (Pharm.), M.D., F.A.A.P. (Editor), Director, The Children's Hospital of Birmingham, Ala.; Associate Professor of Pediatrics, Medical College of Alabama, Birmingham, Ala.; Professor and Chairman, Department of Pharmacology, Howard College, Birmingham, Ala.; member, Revision Committee, and Chairman, Pediatric Panel, Pharmacopeia of the United States. The C. V. Mosby Company, St. Louis, Mo., 1966. 1,223 pages, \$18.50.

**PRINCIPLES OF PATHOLOGY—Second Edition**—Howard C. Hopps, M.D., Chief, Division of Geographic Pathology, The Armed Forces Institute of Pathology. Appleton-Century Crofts, New York, N.Y., 1964. 403 pages, \$8.95.

**PROCEEDINGS OF THE THIRD CONGRESS OF THE ASIAN AND PACIFIC SOCIETY OF HEMATOLOGY**—August 17 to 23, 1964, Jerusalem—Edited by G. Izak, M.D., Associate Professor of Medicine and Head, Hematology Research Laboratory, Hebrew University—Hadassah Medical School, Jerusalem; and Moshe Prywes, M.D., Editor-in-Chief, Israel Journal of Medical Sciences. Grune & Stratton, Inc., New York, N. Y., 1966. 213 pages, \$3.50 (Paperback).

**SHOULDER PAIN**—Rene Cailliet, M.D., Chief of Department of Physical Medicine, Southern California Permanente Medical Group; Associate Clinical Professor, University of Southern California School of Medicine, Department of Physical Medicine and Rehabilitation; and Department Head, Physical Medicine, Kaiser Foundation Hospitals, Southern California. F. A. Davis Company, Philadelphia, Pa., 1966. 115 pages, \$3.00 (Paperback).

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## NEW BOOK

**CURRENT CONCEPTS IN MEDICAL PRACTICE.** Edited by John E. Mullins, M.D. 436 pages. 1965. Mosby. \$10.75. A concise and readable summation of problems commonly met in practice includes new developments which will help to keep up to date.

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## A Drug for Stroke Treatment

Stroke victims showed greater improvement during recent tests when they were given massive doses of a drug which dilates blood vessels of the brain.

The first report of the drug's successful clinical trials on stroke patients appears in the November 29 *Journal of the American Medical Association*.

The authors are John S. Meyer, M.D., Fumio Gotoh, M.D., John Gilroy, M.D., and Nasaharu Nara, M.D., of Wayne State University and Receiving Hospital, Wayne Center for Cerebrovascular Research, and Harper Hospital, Detroit, Mich.

The drug is papaverine hydrochloride, sometimes used as a muscle relaxant, and derived artificially or from opium.

Papaverine was found effective, the report said, by increasing both the blood flow and the amount of oxygen carried by blood to the brain.

One of the difficult problems in treating a stroke patient is maintenance of an adequate blood supply to oxygen-starved parts of his brain.

When a large blood vessel in the brain is blocked, other smaller vessels reroute blood around the obstruction. Often, however, this "collateral circulation" isn't adequate.

Physicians have searched for a substance which would enlarge the cerebral blood vessels, but which would not dilate peripheral vessels.

Clinical trials showed that papaverine does this for extended periods, the authors said.

Such treatment is important immediately after a stroke. Although it is sometimes possible to correct blood vessel blockages, there is evidence that surgery should be deferred for approximately 10 days in cases of acute stroke, the authors said.

Delaying surgery allows anticoagulant treatment of the blood to take effect. It is during this 10-day waiting period that papaverine was found useful in maintaining collateral circulation in the brain.

Seventy stroke patients were treated during the investigation. All received the best medical care available, but in addition, 34 patients were given papaverine. The remaining 36 served as control patients.

At the end of 10 days, 50 patients showed improvement (exactly 25 from each group). By far the greater improvement, however, was among those who received papaverine, the authors said.

Only relatively minor complications were reported. Earlier tests had indicated considerable human tolerance for papaverine.

Papaverine was found particularly effective among older patients. The authors suggested this was because blood vessels of younger persons are already more dilated and thus less responsive to the treatment.



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**References:** 1. Based on 1965 data from independent physicians' market survey organization. 2. Scal, J. C.: Eye Ear Nose & Throat Month. 38:738 (Sept.) 1959.



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**Warnings:** Photodynamic reactions have been produced by tetracyclines. Natural and artificial sunlight should be avoided during therapy. Stop treatment if skin discomfort occurs. No cases of photosensitivity have been reported with Tetrex (tetracycline phosphate complex). With renal impairment, systemic accumulation and hepatotoxicity may occur. In this situation, lower doses should be used. Tooth staining and enamel hypoplasia may be induced during tooth development (last trimester of pregnancy, neonatal period and childhood).

**Precautions:** Bacterial superinfection may occur. Infants may develop increased intracranial pressure with bulging fontanels. In gonorrheal therapy, serologic tests for syphilis should be conducted initially and monthly for 3 months.

**Adverse Reactions:** Glossitis, stomatitis, nausea, diarrhea, flatulence, proctitis, vaginitis, dermatitis, and allergic reactions may occur.

**Usual Adult Dosage:** 1 capsule q.i.d. Continue therapy for 10 days in beta-hemolytic streptococcal infections. Administer one hour before or 2 hours after meals.

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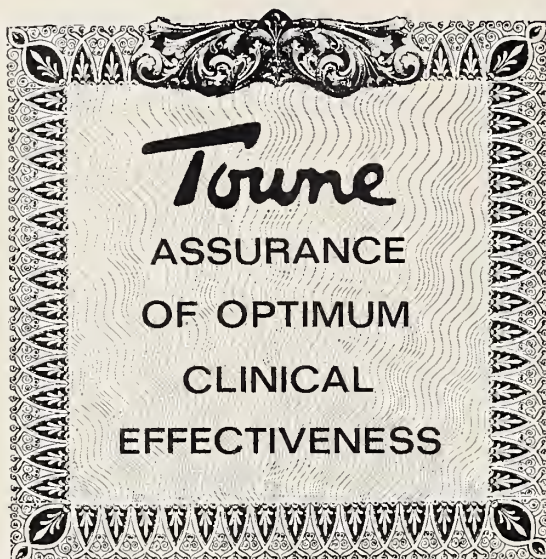
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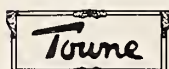


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## Multiple Sclerosis Clusters Found

There appears to be an unidentified environmental factor distributed in much the same way as the clusters of multiple sclerosis found in various countries, says an article in a current publication of the American Medical Association.

Identifying this factor may give a clue to the cause of multiple sclerosis (MS), one of the most common primary diseases of the nervous system.

The unknown factor seems to indicate, the author said, that MS is an "acquired exogenous" disease—meaning one acquired from elements outside the body.

"It would be significant to be able to say that MS is an acquired disease," said an editorial in the February 28 *Journal of the American Medical Association*. "If this concept and the consequent inferences are tenable, a valuable tool in work with the disease may exist."

Up to now, the illness has generally been considered of unknown cause, unpredictable course, and unresponsive to therapy.

The author, J. F. Kurtzke, M.D., summarizes recent studies of the incidence of multiple sclerosis. His report appears in the February issue of the *Archives of Neurology*. Dr. Kurtzke is a staff member of the Veterans Administration Hospital and the Georgetown University School of Medicine, Washington, D.C.

Multiple sclerosis incidence varies in wide bands across the earth, he noted. The northern United States, southern Canada, and northern Europe are in the highest-frequency band (30 to 60 cases of MS per 100,000 population).

Medium-frequency zones (five to 15 per 100,000) include the southern U.S., southern Europe, and Australia. Asia and Africa seem to have the lowest incidence of MS. These figures may be distorted by a lack of adequate surveys in some areas.

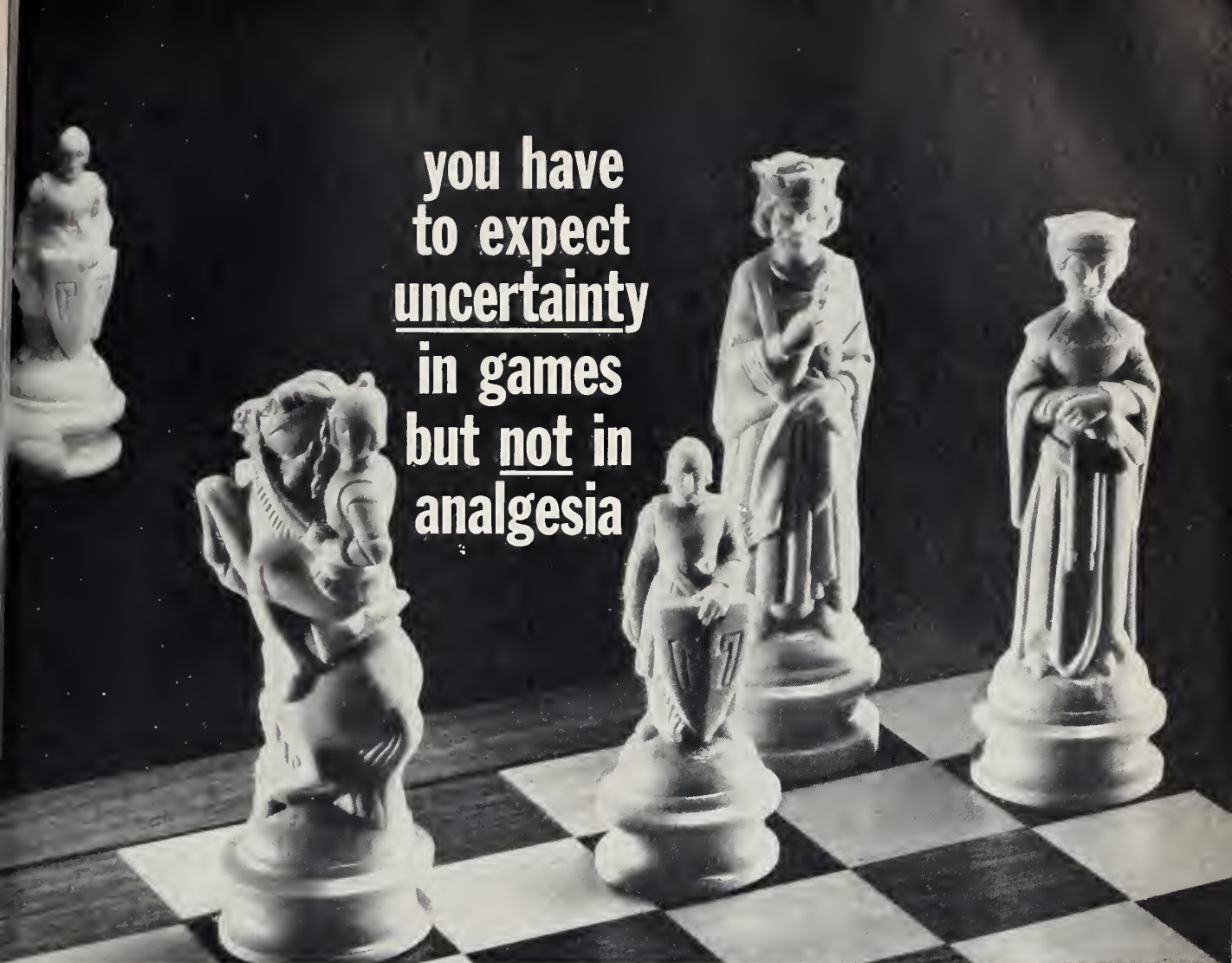
More important, Dr. Kurtzke noted that in almost every North European country where MS has been surveyed, the disease appears in clustered areas.

Dr. Kurtzke concludes that these clusters indicate the presence of an exogenous, or outside, factor associated with the disease. He does not speculate what this factor might be, but does eliminate some possibilities.

Climate or diet seem to be ruled out. The clusters of disease are too small to be affected by these, he said.

Heredity may not be a factor, either. In Denmark and Switzerland, where two generations of patients were surveyed, MS could not be attributed to familial cases. Neither could it be correlated with the distribution of doctors or medical facilities.





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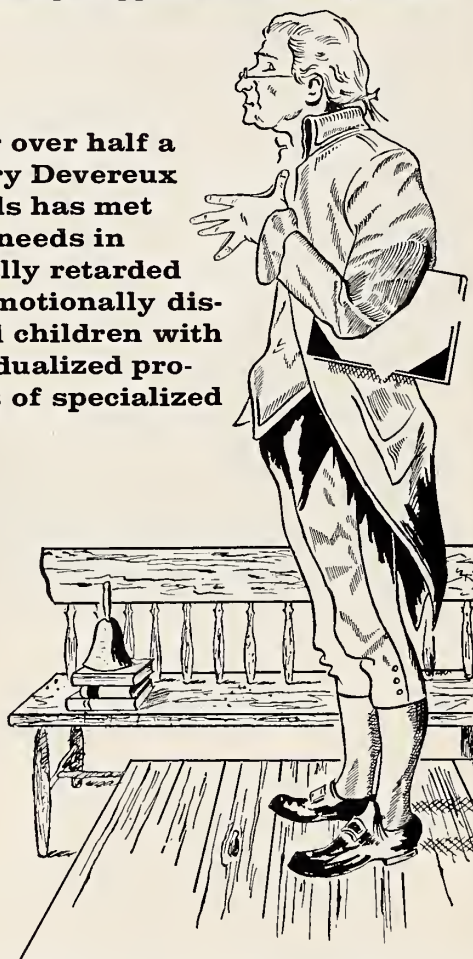
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## Blue Shield Third Quarter Enrollment Hits New High

Membership of the 85 Blue Shield Plans in the United States, Canada, Puerto Rico, and Jamaica increased 1,029,265 during the first three quarters of 1965 to a record 57,286,041, the National Association of Blue Shield Plans reported.

Over half of the increase, 549,602, was acquired in the second quarter. The addition of a new Plan—Windsor, Ontario—contributed 263,445 members to the second quarter gain.

Included in the total enrollment figure is the membership of Medical Indemnity of America, Inc., a stock company wholly owned by the National Association of Blue Shield Plans.

During the first nine months of 1965, membership gains were reported by 63 Plans, 20 had losses, and two remained the same. Gains totaled 1,340,577, while losses amounted to 311,312.

Third quarter gains of 438,856 were posted by 56 Plans, with 26 Plans reporting losses of 129,412. Three Plans showed no change.

The 1.83 per cent enrollment increase in the first nine months brought Blue Shield coverage in the United States to 27 per cent of the population.

Blue Shield now covers 26.8 per cent of the Canadian population, 1.4 per cent of the Jamaican population, and 4.1 per cent of the population of Puerto Rico.

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## Contact Lenses and Eye Complications

Fourteen eyes had to be removed or were blinded and 157 eyes were permanently damaged within one year among approximately 50,000 contact-lens wearers, a national survey reports.

The survey, conducted by the American Association of Ophthalmology is reported in the March 14 *Journal of the American Medical Association*.

There also were 7,607 "reversible ocular changes" among the 49,954 persons examined. These were eye changes from which patients recovered without permanent defects.

"The popularity of contact lenses has exceeded the public knowledge of potential hazards associated with their use," said the Committee on Contact Lenses of the AAO.

The report listed precautions for contact-lens wearing, and suggested responsibilities of ophthalmologists in fitting the lenses. It made no recommendations, however, concerning the relative merits of the various kinds of contact lenses or conventional glasses.

Eye complications associated with contact lenses are more frequent among older persons and those with previous eye injuries or disease, the report said. Complications also are associated with prolonged wearing or with sleeping with the lenses on the cornea. Eye problems are made more severe by wearing the lenses after the complications appear, the report said.

The survey consisted of questionnaires mailed to 8,181 ophthalmologists. A total of 1,904 returned answers concerning 49,954 patients seen in the 12 months prior to April 1960.

Infection was present in each of the 14 reported cases of eye loss or blindness. In four cases, the infection was due to fungi. In 10 cases, it was bacterial or due to unidentified organisms.

The report pointed out, however, that wearing contact lenses with proper technique on the normal eye does not alter the eye's normal bacterial flora.

Six of the 14 patients required removal of the eye. Two required corneal-graft operations; only one of these recovered vision in the eye, and it was reduced to 20/50.

The only incident of blindness in both eyes caused by contact lenses was reported previously in 1956, and was not included in this report.

Observations made as part of the report are that "the wearing of contact lenses is an abnormal condition which can result in serious medical complications," and that these complications require prompt medical diagnosis and treatment.

"This survey and previously published clinical and laboratory studies suggest that the majority of patients wearing contact lenses have some de-

(Continued on Page 23)

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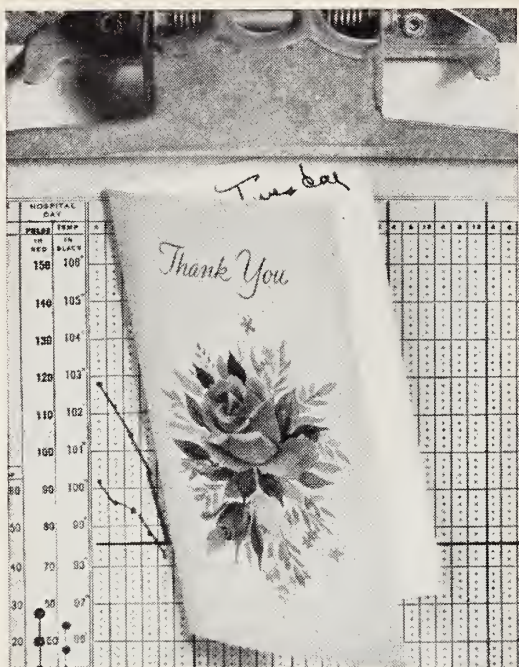
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## Preliminary Report Favorable on New Drug for Gonorrhea

Preliminary tests have been favorable for a new antibiotic used to treat gonorrhea, says a report in the March 14 *Journal of the American Medical Association*.

The drug, cephaloridine, may prove particularly effective in treating persons allergic to penicillin, which is commonly used against gonorrhea. Cephaloridine may also be effective against gonococcal strains that are showing increasing resistance to penicillin.

The *Journal* report is from the Communicable Disease Center of the U.S. Public Health Service, Atlanta, and the Fulton County (Atlanta) Health Department.

A cure rate of between 88 and 98 per cent was obtained when 84 male patients were given a single intramuscular injection of the drug. (Doctors aren't sure of the exact cure rate because about half the men didn't return for a checkup. Three who did return had probable reinfections.)

Stressing that this is a preliminary report, the authors point out that larger numbers of patients, including women, now need to be tested. These early results, however, suggest that cephaloridine was effective and produced little, if any, allergic reaction.

Cephaloridine has been produced in England and has been the subject of several favorable clinical reports there, the *Journal* article said.

Advantages of cephaloridine over a related drug, cephalothin, include a longer level of effectiveness in the blood, greatly increased solubility, and freedom from pain on injection.

"The control of gonorrhea remains a difficult problem in the United States, and estimates place the number of newly acquired cases at over one million yearly," the report said.

"Many reports during the past 10 years have demonstrated an increasing resistance of gonococci to penicillin. This has required that penicillin dosages be increased periodically to maintain satisfactory cure rates.

"While estimates vary widely, it is generally conceded that 5 to 10 per cent of the population is now allergic to penicillin in some manner. Many of these patients receive therapy with alternate and often less effective antibiotics.

"Thus, the search for newer antimicrobial agents useful in the control of gonorrhea becomes increasingly urgent," the report said.

Authors of the report are James B. Lucas, M.D., and James D. Thayer, Ph.D., of the Public Health Service, and Phillip M. Utley, M.D., Terrence E. Billings, M.D., and James E. Hackney, M.D., of the Fulton County Health Department.



# Results of Psychotherapy

NORMAN Q. BRILL, M.D., *Los Angeles*

■ *A controlled double blind study was made of 299 non-psychotic female psychiatric clinic patients divided into six groups, with members of each group dealt with in a different manner from those in other groups. Those in one group had one or two hour-long psychotherapy sessions a week. Four groups were limited to brief visits but were given one of three kinds of drugs or a placebo. One group was merely put on a waiting list and received no therapy. As determined by a variety of independent measures, there was a fairly uniform average improvement of all groups except the one that received no treatment. Follow-up 10 to 18 months after termination of treatment revealed that the average patient had maintained her improvement and that those who had received no treatment showed considerable improvement after they were removed from the waiting list.*

*The findings suggested that the widespread preference for the traditional outpatient psychotherapy is based as much on the physician's bias as on proven greater effectiveness over briefer treatment methods. There was some confirmation that many things other than the development of understanding enter into much of the so-called psychoanalytically oriented psychotherapy and may have profound effect on the outcome.*

PSYCHIATRISTS WHO DO a considerable amount of psychotherapy prefer to think that they are being "scientific" in what they do, especially when using psychoanalytically oriented techniques. They believe this because these techniques are based on a comprehensive theory of personality development which lends itself to predicting behavior; and because the techniques are designed to help a person to understand the forces and unconscious origins of his emotional difficulties and thus help

him change his way of reacting by giving proper value to rational considerations. There is a tendency for such psychiatrists to place a great reliance on what they do whether it is interpreting, clarifying, helping a patient to abreact or to understand his conflicts and fears; and there is a tendency to assume that the results of their treatment are primarily a function of these elements in their techniques.

However, it cannot be denied that the roots of psychotherapy are in the ancient practices of priests and witch doctors and its effectiveness seems to rest in part on the power of suggestion and on the ability of a person accorded special

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Submitted October 8, 1965.

power or status to influence others who wish to be influenced.

Submitting oneself to another's influence and the underlying need for this in a person are looked down upon in our culture as manifestations of weakness, or inadequacy, and to some extent result in critical or belittling remarks being directed to the patient, to the psychiatrist-doctor and to the procedure. This belittling and skeptical attitude toward psychotherapy also tends to be extended to or displaced upon the results of such treatment and leads to remarks like "no one is really helped," despite the fact that there are many reported studies and testimonials to its effectiveness.

### Variables in Psychotherapy

Reported studies, however, are often not comparable because of differences in techniques that were used. In attempting to define the nature of the modern psychotherapeutic process, an investigator is confronted by an almost limitless number of variables which enter into the interaction between therapist and patient and by a lack of yardsticks to measure these variables. From experiments in which therapists have been observed while treating patients (and especially private patients) it seems that what they *report* they do differs a good deal from what they *do* do. Greater significance is usually attached to remarks and silences, interpretations and encouragement, than to the fact that this patient was selected for treatment rather than some other patient; that a great effort is made to avoid any interruption of a session except in an emergency; that all attention is focused on the patient with a sympathetic understanding manner that is real or studied.

Young male psychiatrists, if given the choice, tend to select women rather than men, younger ones rather than older ones, and attractive ones rather than unattractive ones. They tend to choose patients who somehow convey an impression of readiness to receive help (or be influenced) and to accept for treatment patients with mild disability rather than those with severe disability. In general, they prefer patients they like and their reluctance to be observed while treating a patient is often greater than that which is seen in the patient. The reluctance at times approaches that which would be expected in situations involving some very highly personal activity.

### Problems in Evaluating Results

Not only do different studies employ different measures of results, but even when measures are the same they may not be reliable. One cannot rely on just change in symptoms, since treatment may relieve a patient of a phobia but disrupt his marriage, or be complicated later by the development of a peptic ulcer. Or, a patient may overcome sexual frigidity but develop severe hypertension in its place.

How can understanding be measured? How can change in attitudes be accurately defined when it may take years merely to learn of their existence? What is a reliable measure of disability that can be used for the artist as well as for the bookkeeper, and how may interpersonal relationships which can vary from week to week and year to year be quantified? Does one consider immediate effects or only those which persist?

It is literally impossible to control for all variables without using some fantastically large sample that would permit the isolation of identical groups of patients who were matched not only for diagnosis, age, sex, education, intelligence, duration and severity of illness, symptoms, previous treatment and physical condition, but also for the more subtle but equally critical characteristics of motivation, personality, psychological mindedness, ego strength, expectation of help, current life situation, individual defenses and psychopathology.

### Results of a Controlled Comparative Study

Despite all of these difficulties, we did not undertake a study of outpatient treatment.\* In view of all the glowing reports on the use of tranquilizers, we wondered if a more economical treatment than the psychoanalytically oriented psychotherapy being used in our clinic was truly available. While our study employed criteria of change that are not totally comparable with criteria used in other studies, it permitted the comparison of different methods of treatment on groups of patients that were reasonably comparable.

From 1958 to 1963 we carried out a controlled study, double blind so far as drug therapy was concerned, on 299 non-psychotic female outpatients who, if there had been no limitation of staff, would in all likelihood have been treated

\*The study is described in detail in *The Archives of General Psychiatry* Vol. 10, pp. 581-595, June, 1964. There will be no repetition here of the criteria used in the selection of patients, or of the details of the methods used in the study. It was supported by USPHS Grant No. MY-2923 from the National Institute of Mental Health.



with psychotherapy that involved an hour visit once or twice a week for many months. Instead, they were assigned at random to one of six groups. The patients in one group received psychotherapy of the kind the vast majority of clinic patients were getting. Those in three of the groups were limited to visits of 10 to 15 minutes a week and one of the three groups received meprobamate, another prochlorperazine and the third phenobarbital. Another group was also limited to the short visits but received an inactive placebo instead of one of the drugs. The last group was placed and maintained on a waiting list without treatment.

Following a treatment period or waiting period of from two to 12 months, each patient was re-evaluated clinically by several different persons and by means of a battery of psychological tests. In addition, the patient and her husband or close relative independently reported the results of treatment. The psychotherapy group was in active treatment for an average of five months. The average length of treatment for the patients treated with drugs was four months; they, of course, were seen less frequently and their sessions were limited to 10 to 15 minutes.

The characteristics of the patients assigned to the six groups were determined by several tests and when the groups were compared on the basis of these measures, no statistically significant differences were found.

Dropouts occurred in all groups. The proportion varied from 36 per cent in the meprobamate

group to 50 in the prochlorperazine group, but no statistically significant differences were found among the six groups (Table 1).

The initial psychological test scores of those who completed treatment were found to be comparable to those of the dropouts. The small differences which were present were insufficient to introduce any important bias into the interpretation of results.

There was no particular diagnostic category which was significantly over-represented in the dropout group, although variations did occur.

The outstanding finding was the fairly uniform average improvement of all groups except the waiting list. This was seen in the estimate of change in patients' symptoms made by the physician and in Minnesota Multiphasic Personality Inventory (MMPI) profiles at the termination of treatment.

On a 16-item evaluation form filled out by the physician, no statistically significant differences among the treatment groups were seen (Chart 1). The psychotherapy group was rated slightly better on "ability to work effectively" and on "understanding of self." The latter rating probably to some extent reflected the prejudice of the physician regarding psychotherapy.

The patients, too, rated the change in their conditions. On almost all items those who received meprobamate reported more improvement than those who were treated with psychotherapy or other drugs (Chart 2). The difference has statis-

TABLE 1.—Distribution of "Dropouts" by Treatment Group

Treatment Group	Number Assigned	Number Retested	Number Dropped Out	Per Cent Dropped Out
Meprobamate .....	53	34	19	36
Placebo .....	55	30	25	45
Phenobarbital .....	53	28	25	47
Prochlorperazine .....	54	27	27	50
Psychotherapy .....	50	30	20	40
Waiting List .....	34	20	14	41
Total .....	299	169	130	43.5

$\chi^2=2.85$ ,  $df=5$ . Differences in percentages are not statistically significant.

TABLE 2.—Patient's Response at Termination to the Question: "Do You Feel That You Have Been Helped by Treatment? (in General)"

	Treatment Group					Total
	Psychotherapy	Meprobamate	Placebo	Phenobarbital	Prochlorperazine	
Helped very much.....	19	20	11	10	7	67
Helped somewhat .....	6	8	16	11	17	58
No change .....	1	2	3	5	3	14
Worse than before treatment.....	1			2	1	4
(No information) .....	23	23	25	25	26	122
Total .....	50	53	55	53	54	265

CHART 1.—RATINGS BY RESIDENT AT TERMINATION

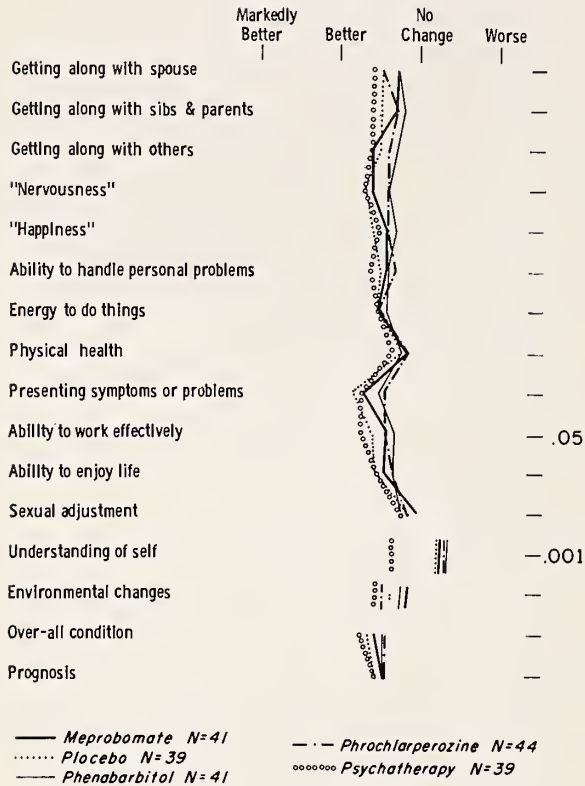
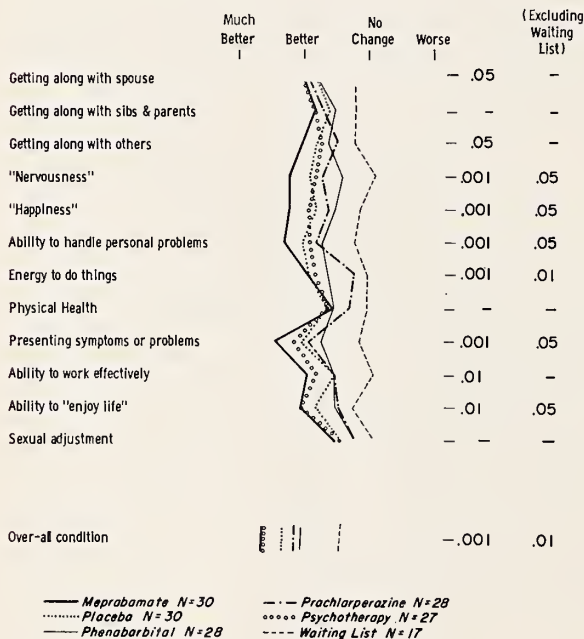


CHART 2.—RATINGS BY PATIENT AT TERMINATION



tical significance when this group is compared with the waiting list group that received no treatment. The rating of "overall condition" summarizes the results; here the meprobamate and psychotherapy groups are rated significantly more improved than the others. The patients' rating of effect of treatment is given in Table 2. It is of interest that they tended to consider themselves more improved than did their physicians. Relatives, too, tended to rate patients as more improved than did the physicians, and the ratings of relatives paralleled the meprobamate patients' more favorable reports. The psychotherapy group occupies an intermediate position.

Similar independent ratings were made by a social worker who compared social work evaluations that were made before and after treatment. The social worker making the rating had not seen any of the patients, but only the written reports. Her findings were consistent with the others.

We determined the attitude of the physicians toward psychotherapy and drug treatment. No correlation between attitude and treatment outcome was found. This was an unexpected finding, and it may be that our measuring instrument was not sufficiently sensitive.

Follow-up 10 to 18 months after termination of treatment revealed that the average patient had maintained her improvement. In fact, the average scores on almost all measures indicated some additional improvement. The waiting-list group showed the greatest average improvement during the follow-up period although it was still the lowest group. The differences between it and the treatment groups were much smaller than before and statistically not significant. There were now no differences among the drug and placebo groups, except perhaps for a tendency of the prochlorperazine-treated group to remain lowest. Psychotherapy patients fairly consistently had a slight (but statistically insignificant) edge over other treatment groups; this difference was overshadowed by the unexpectedly good results in most patients, regardless of treatment they had received.

## Conclusions

The effect or lack of effect of the drugs used cannot be attributed solely to the drugs, since all patients who received drugs also received some sort of psychotherapy—generally as much as the physician was able to squeeze into the 10 or 15 minutes he was with the patient. In addition, the



mere prescribing of a drug without any planned psychotherapeutic interaction has meaning for the patient which will vary with the attitude and manner of the physician prescribing the drug and the nature of his relationship to the patient.

The results showed that many of the clinic patients studied did as well with relatively brief treatment interviews (10 to 15 minutes) supplemented by the judicious use of mild or innocuous medication, as they did with weekly psychotherapy sessions of one hour each over a long period. These findings were unexpected. They suggest that the widespread preference for the traditional outpatient psychotherapy is based as much on the physician's bias as on its proven greater effectiveness. There is some confirmation of the assumption that many things other than the development of understanding enter into much of the psychoanalytic psychotherapy that is practiced, and may have profound effects on the outcome. There is perhaps much more suggestion, more transference, more identification and more direct gratification of patients' need than we like to believe is the case.

However, as we have pointed out elsewhere, the study was not designed to detect the kind of subtle changes in attitudes which might uniquely occur with long-term, intensive psychotherapy, nor was it intended to define the really long-term results of treatment. Psychiatric residents, not experienced senior staff members, administered all treatment.

The findings do not justify any departure from the principle of providing treatment which is based on an understanding of psychodynamics and unconscious factors in emotional illness. Nor did the results of the study warrant discontinuing the use of intensive psychotherapy or psychoanalysis for types of disorders for which these are shown to be particularly indicated. Psychotherapy should be regarded as many things rather than just one thing. It is a procedure which should not be recommended without qualification, nor undertaken without clear definition of goals. Much research remains to be done to establish the indications for the various types of psychotherapy and to measure the long-term effectiveness.

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# Goals for California Against Cancer

LESTER BRESLOW, M.D., *Berkeley*

■ *Assuming that present trends continue, about 30,000 persons in California will be dying from cancer each year by the early 1970's. This expectation takes into account both changes in the size and other characteristics of the population, and changes in cancer mortality rate—increases in some sites and decreases in others, according to the 1950-1960 trends.*

*On the other hand, if everything now known to avoid cancer deaths were actually done, conservative estimation indicates that each year at least 7,500 of the 30,000 expected cancer deaths (based on the trends of 1950-1960 and taking into account present accomplishment as well as failure) would not occur. Possibly many more deaths could be avoided.*

CANCER IS PROPERLY regarded as a biological phenomenon. Neoplastic, and sometimes fatal, growth of cells in various tissues occurs throughout the biological world. Manifestations of this phenomenon tend to be specific for each species. For example, man now suffers predominantly from lung cancer; certain breeds of cattle are prone to cancer of the eye; dogs are affected particularly by a neoplastic growth of the anal region; leukemia-like diseases are known to affect mice, chickens, dogs, man and dairy cattle. Although cancer remains largely an enigma, knowledge of causative factors is growing rapidly—paralleling the increase in resources for research. Already it is clear that physical, chemical, genetic, viral and possibly other influences are involved.

Besides being viewed in its biologic aspects, cancer may also be considered as a social disease. Like other social diseases cancer arises out of the conditions of life. Every period and locale of human life is characterized by a pattern of disease, a pattern which changes with conditions of life.

The occurrence of cancer is consistent with this general rule.

A young man working as a chimney-sweep in London during the early 19th century was likely, in time, to have cancer of the scrotum. A young man of the 20th century living in California would not be likely to have cancer of the scrotum; but if he acquires the common habit of smoking cigarettes at a young age and smokes heavily, he is likely sooner or later to have lung cancer. A middle-aged woman born in Alabama who began having her children before the age of 20 is at high risk for cancer of the cervix. She may be working as a domestic in the home of an upper-class woman in Beverly Hills; her employer would face less likelihood of cancer of the cervix, but she is at greater risk than her domestic helper to have cancer of the breast.

Variations in conditions of life are the main determinants of the occurrence of cancer and the outcome of the disease. This may be illustrated by Chart 1 which shows the mortality trend in California over a single generation, 1930-1964, for

From the State of California Department of Public Health.  
Submitted 15 October 1965.



several of the major sites of cancer in men and women.

Stomach cancer is fast disappearing in California (and in the United States). Among both males and females, mortality from stomach cancer has declined about two-thirds since 1940, and it now appears to be receding into the older age groups, especially those born in other countries. Although the death rate from the disease is falling, we do not know why. Incidentally, this decline is not experienced in certain other countries; for example, in Japan stomach cancer continues at a high rate.

In sharp contrast, lung cancer has been increasing rapidly during this same period, particularly among American and European men. A rare type of cancer only a generation or so ago, lung cancer has become the leading fatal cancer among men in Western countries, and it is now also increasing among women there. Lung cancer already accounts for about one-sixth of all deaths from cancer in California and the proportion will increase to become one-fourth of all cancer deaths within another decade if present trends continue. The major factor in this tremendous rise is now well established as cigarette smoking, which has become a common practice in our time and place of life.

Among American women, breast cancer results in a high mortality rate in spite of intensive medical and educational efforts (Chart 1 and Tables 3 and 4). Death rates for breast cancer in California women increased from 1910 to 1940, but have been declining steadily since then—from a high point of 28 per 100,000 in 1940 to 22 in 1964. Whether current improvements in diagnosis and treatment as well as public understanding of the disease will effect a more rapid reduction in mortality rate from breast cancer remains to be seen.

Cancer of the uterus in California (and in the United States generally) has shown a substantial decline, associated with earlier casefinding and more effective treatment. During the past decade or so, the cytologic test for cancer of the cervix (Papanicolaou smear) has apparently accelerated progress against cancer of the uterus.

Many factors are thus at work influencing the occurrence and outcome of cancer. Some of these are environmental and can be controlled by such measures as, for example, industrial hygiene in the case of certain forms of bladder cancer. Others must be approached at the present state of knowledge through a change in personal habits, particu-

larly cigarette smoking for lung cancer. Medical care is another influence to be considered in the attack on cancer, and it is a factor of growing importance as advances are made in medical science and practice.

In the long run, the cancer problem will probably be solved through insight into the biological aspects of the phenomenon. Knowledge of the mechanism by which cells become neoplastic and of the agents which trigger this mechanism is most likely to lead to the ultimate solution.

Research to gain this insight must therefore continue to receive high priority in cancer control efforts. Cancer research is especially promising at the present time when virologists, chemists, geneti-

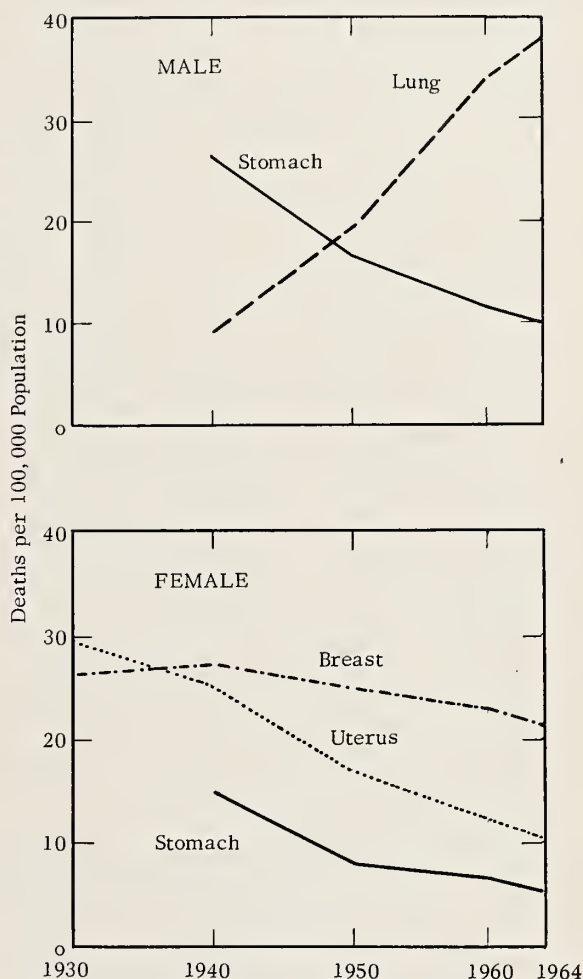


Chart 1.—Age-adjusted cancer death rates,<sup>1</sup> selected sites for each sex, in California, 1930-1964.

<sup>1</sup> The indirect method of adjustment was used with United States 1940 rates taken as the standard.

Source: National Office of Vital Statistics: *Vital Statistics of the United States, 1910-1940* and unpublished tabulations; U.S. Bureau of the Census: *Vital Statistics of the United States, 1900-1940*; California, State Department of Public Health, Death Records.

TABLE 1.—Population and Cancer Deaths by Site, in California, 1950, 1960, and 1964

	1950	1960	1964
<i>Population</i>			
Both Sexes.....	10,586,223	15,717,204	17,947,000 <sup>a</sup>
Male .....	5,295,629	7,836,707	8,780,000 <sup>a</sup>
Female .....	5,290,594	7,880,497	9,167,000 <sup>a</sup>
<i>Number of Cancer Deaths</i>			
All Sites.....	14,963	22,051	24,897
Lung .....	1,418	3,239	4,206
Stomach .....	1,562	1,637	1,566
Large intestine.....	1,452	2,083	2,333
Rectum .....	682	932	958
Pancreas .....	698	1,160	1,374
Breast .....	1,571	2,116	2,340
Cervix uteri.....	601	705	688
Uterus, other than cervix.....	454	379	405
Ovary .....	472	679	749
Prostate .....	735	1,056	1,130
Kidney .....	267	394	494
Bladder .....	510	646	674
Leukemia .....	653	1,071	1,196
All other sites.....	3,888	5,954	6,784

<sup>a</sup> Projected civilian population.

Source: U.S. Bureau of Census: *Census of Population, 1960: California*, Washington, 1962; California, State Department of Finance: *California Population—1963*, Sacramento, 1963; California, State Department of Public Health, Death Records.

TABLE 2.—Number of Cancer Deaths, Selected Sites, by Sex, in California, 1910-1964

Site and Sex	1910	1920	1930	1940	1950	1960	1964
All Sites <sup>1</sup> .....	2,013	3,874	7,170	10,128	14,130	20,711	23,420
Male .....	862	1,846	3,355	4,938	7,084	11,036	12,464
Female .....	1,151	2,028	3,815	5,190	7,046	9,675	10,956
Buccal Cavity and Pharynx.....	92	148	279	311	361	546	607
Digestive Organs and Peritoneum.....	1,070	2,006 <sup>a</sup>	3,462	4,404	5,192	6,919	7,474
Male .....	508	1,111	1,924	2,493	2,913	3,820	4,031
Female .....	562	895	1,538	1,911	2,279	3,099	3,443
Stomach .....	b	b	1,566 <sup>c</sup>	1,673 <sup>c</sup>	1,562	1,637	1,566
Male .....	b	b	b	1,055 <sup>c</sup>	1,006	987	965
Female .....	b	b	b	618 <sup>c</sup>	556	650	601
Female Genital Organs.....	281	525	1,017	1,356	1,575	1,820	1,917
Uterus .....	b	481	845	1,006	1,055	1,084	1,093
Cervix .....	b	b	b	b	601	705	688
Breast <sup>2</sup> .....	170	370	750	1,126	1,571	2,116	2,340
Respiratory System .....	b	b	296	691	1,614	3,498	4,488
Male .....	b	b	216	535	1,322	2,943	3,666
Female .....	b	b	80	156	292	555	822
Trachea, bronchus and lung.....	b	b	b	525	1,418	3,239	4,206
Male .....	b	b	b	395	1,161	2,725	3,448
Female .....	b	b	b	130	257	514	758
Other and Unspecified Sites.....	440 <sup>d</sup>	825 <sup>d</sup>	1,366	2,240	3,817	5,812	6,594

<sup>1</sup> Excludes Hodgkin's disease and leukemias.

<sup>2</sup> Includes a few male deaths.

<sup>a</sup> Excludes pancreas, esophagus and unspecified digestive organs.

<sup>b</sup> Deaths are not separately classified.

<sup>c</sup> Includes duodenum.

<sup>d</sup> Includes respiratory system and liver.

Source: National Office of Vital Statistics: *Vital Statistics of the United States, 1910-40* and unpublished tabulations; U.S. Bureau of the Census: *Vital Statistics Rates of the United States, 1900-40*; California, State Department of Public Health, Death Records.

cists, epidemiologists and others are collaborating in the attack. Terms such as *cyto-genetics*, *immuno-chemistry* and *molecular-biology*, and events such as the elucidation of the viral pathogenesis of leukemia in chickens by a veterinarian working in association with a man trained as a chemist, indicate both the nature of cancer's complexity and

how it is being approached through the growth and merging of several sciences.

In the meantime, the nation and each state can set goals against cancer for accomplishments within the framework of present knowledge. These goals will, of course, be extended as new knowledge accumulates. However, we already know



much that could be used more aggressively today in the control of cancer: curtailment of cigarette smoking; occupational hygiene and other measures to avoid environmental agents that have been demonstrated to produce cancer; medical care, particularly that directed toward early detection and prompt treatment of cancer. Education, environmental measures and medical care should be expanded to reach all who might benefit, closing the gap between what is known to be feasible and what is actually being accomplished at present.

### Present Status of the Cancer Problem

Cancer has advanced in its relative position as a cause of death—from being responsible for only one out of 25 deaths at the turn of the century, to about one out of six deaths today. Each year now about 25,000 persons in California die of cancer. However, the vista is not entirely grim. The age-adjusted mortality rate from cancer as a whole has already declined about one-fourth among women during the last generation, due both to some as yet little-understood changes in conditions of life and to certain improvements in medical care. Except for the phenomenon of lung cancer, the total mortality rate for cancer among men would also have fallen (Table 4).

Already the commonest of fatal cancers and the most rapidly increasing, *lung cancer* now causes more than 4,200 deaths in California annually. Tables 2, 3 and 4 show the rapid increase in deaths from lung cancer during recent years. At this rate of increase lung cancer will be responsible for about 7,500 deaths in California, each year, by the early 1970's. If present trends continue, more than 100,000 children of school age now living in California will die of lung cancer before reaching 70 years of age. It is overwhelmingly clear that the major factor in the phenomenal rise in lung cancer is cigarette smoking. The report of the Surgeon General's Advisory Committee summarizes the evidence on this issue. Without control of cigarette smoking there is no present hope of reducing the still rising toll among men or of averting the already starting substantial rise among women, as the impact of cigarette smoking among women during the past few decades begins to manifest itself as disease in the 1960's and 1970's. Those who have never smoked cigarettes have only one-tenth the likelihood of lung cancer that persons who do smoke them have. For those who now smoke cigarettes, cessation greatly reduces the

likelihood of lung cancer. It is to be hoped that the decline in cigarette smoking among physicians presages what can be accomplished in the general public.

*Cancer of the gastrointestinal tract* including its auxiliary organs accounts for about one-third of all deaths from cancer.

As noted earlier, stomach cancer has fallen off dramatically, both as a cause of death (Table 4) and in incidence (Table 5). The drop in stomach cancer death rate is due largely to a drop in frequency of occurrence rather than to accomplishment of medical care in cases after the disease has started. Although some improvement in medical care has taken place, patients with stomach cancer still have only about a 10 per cent survival (measured as five-year relative survival rate, which is computed by adjusting the observed survival rate for normal life expectancy). Presumably some change in the conditions of life is responsible for the decline, possibly diet or other characteristics that distinguish the low income group of the population, known to have an excessively high frequency of stomach cancer, from the rest of the population. The fact is that we have no explanation for the rapid decrease in this disease.

Cancer of the large intestine accounts for about one-third of deaths from gastrointestinal tract cancer. The five-year relative survival rate among patients with cancer of the large intestine (all stages combined) is now about 34 per cent for males and 40 per cent for females (Table 6). These figures are based upon the experience of patients admitted with all stages of cancer of the large intestine to fairly typical hospitals in California during 1952-1956. Data for Tables 6 to 11 are taken from the California Tumor Registry, particularly a monograph based on 110,229 cancer cases, titled *Cancer Registration and Survival in California, 1963*.

Several facts suggest that full application of the present diagnostic and therapeutic knowledge could yield further substantial improvement in the five-year relative survival rate from cancer of the large intestine. These facts include: (1) the approximately 50 per cent improvement in survival from 1942-1946 to 1947-1951 has held firm to the present; (2) an increasing proportion of patients are receiving definitive and successful surgical treatment; and (3) patients in private hospitals are having much better survival experience

TABLE 3.—Crude Cancer Death Rates, Selected Sites, by Sex, in California, 1910-1964

Site and Sex	1910	1920	1930	1940	1950	1960	1964 <sup>e</sup>
All Sites <sup>1</sup> .....	84.7	113.0	126.3	146.6	133.5	131.8	130.5
Male .....	65.2	101.8	114.0	140.5	133.8	140.8	142.0
Female .....	109.1	125.7	139.5	153.0	133.2	122.8	119.5
Buccal Cavity and Pharynx.....	3.9	4.3	4.9	4.5	3.4	3.5	3.4
Digestive Organs and Peritoneum.....	45.0	58.5 <sup>a</sup>	61.0	63.8	49.0	44.0	41.6
Male .....	38.4	61.3	65.4	70.9	55.0	48.7	45.9
Female .....	53.3	55.5	56.2	56.3	43.1	39.3	37.6
Stomach .....	b	b	27.6 <sup>c</sup>	24.2 <sup>c</sup>	14.8	10.4	8.7
Male .....	b	b	b	30.0 <sup>c</sup>	19.0	12.6	11.0
Female .....	b	b	b	18.2 <sup>c</sup>	10.5	8.2	6.6
Female Genital Organs.....	26.6	32.5	37.2	40.0	29.8	23.1	20.9
Uterus .....	b	29.8	30.9	29.7	19.9	13.8	11.9
Cervix .....	b	b	b	b	11.4	8.9	7.5
Breast <sup>2</sup> .....	16.1	22.9	27.4	33.2	29.7	26.9	25.5
Respiratory System .....	b	b	5.2	10.0	15.2	22.3	25.0
Male .....	b	b	7.3	15.2	25.0	37.6	41.8
Female .....	b	b	2.9	4.6	5.5	7.0	9.0
Trachea, bronchus and lung.....	b	b	b	7.6	13.4	20.6	23.4
Male .....	b	b	b	11.2	21.9	34.8	39.3
Female .....	b	b	b	3.8	4.9	6.5	8.3
Other and Unspecified Sites.....	16.8 <sup>d</sup>	24.1 <sup>d</sup>	24.1	32.5	36.0	37.0	36.7

<sup>1</sup> Excludes Hodgkin's disease and leukemias.<sup>2</sup> Includes a few male deaths.<sup>a</sup> Excludes pancreas, esophagus and unspecified digestive organs.<sup>b</sup> Deaths are not separately classified.<sup>c</sup> Includes duodenum.<sup>d</sup> Includes respiratory system and liver.<sup>e</sup> Projected civilian population in California 1964 used to calculate rates.Source: National Office of Vital Statistics: *Vital Statistics of the United States, 1910-40* and unpublished tabulations; U.S. Bureau of Census: *Vital Statistics Rates of the United States, 1900-40*; California, State Department of Public Health, Death Records.

than are patients in county (public) hospitals (Table 10).

The outlook with respect to cancer of the rectum is quite similar to that of cancer of the large intestine. Based upon the same considerations and similar improvement—the five-year relative survival rate for 1952-1956 was 38 per cent for males and 40 per cent for females—it seems reasonable to seek a sizable reduction of the present mortality rate (Table 6).

Pancreas cancer also is a prominent component of gastrointestinal tract cancer mortality. Unhappily, however, data from the tumor registry indicate that fewer than 2 per cent of patients with this disease survive five years. Cancer of the pancreas is difficult to diagnose before disease is well advanced, and little can be accomplished with present means of therapy.

*Cancer of the breast*, from the standpoint of its mortality trend during recent decades, presents a rather baffling situation. The overall mortality rate from cancer at this site rose gradually until 1940, but in California it has definitely tapered off since then. In 1964, the age-adjusted death rate for cancer of the breast fell to 22 per 100,000 population from a high of 28 in 1940.

Perhaps it is time to throw off the attitude of defeatism regarding diagnosis and therapy in cancer of the breast which has pervaded clinical circles. While the data certainly do not justify the kind of optimism which now prevails with respect to cancer of the uterus, there are grounds for guarded optimism with respect to cancer of the breast. The five-year relative survival rate for breast cancer (all stages) in California rose from 51 per cent in 1942-1946 to 58 per cent in 1947-1951 and remained essentially unchanged during the ensuing five years (Table 6). More recent data for 1955-1959 indicate further improvement in survival. During the period 1942-1956, 44 per cent of breast cancer patients admitted to private hospitals had their disease diagnosed while it was still in the localized stage; however, in only 25 per cent of patients admitted to public hospitals was it diagnosed at so favorable a time (Table 8).

An 82 per cent five-year relative survival rate can be expected in localized cancer of the breast (Table 7), compared with 58 per cent for cancer of the breast, all stages combined (Table 6). More than three-fifths of the patients with breast cancer admitted to private hospitals survived at least as long as five years (taking account of normal life



TABLE 4.—Age-Adjusted<sup>1</sup> Cancer Death Rates, Selected Sites, by Sex, in California, 1910-1964

Site and Sex	1910	1920	1930	1940	1950	1960	1964 d
All Sites <sup>2</sup>	96.7	116.6	123.9	126.1	115.3	116.6	114.0
Male	71.8	102.3	112.6	124.2	119.6	131.4	129.8
Female	130.6	133.6	136.3	128.5	111.9	104.2	100.9
Buccal Cavity and Pharynx	4.6	4.5	4.9	3.9	2.9	3.0	3.0
Digestive Organs and Peritoneum	52.3	61.1 <sup>a</sup>	60.2	54.4	41.7	38.2	35.8
Male	42.5	61.7	64.6	62.6	49.1	45.4	41.9
Female	66.1	60.7	55.6	46.6	35.3	32.0	30.2
Stomach	b	b	27.3 <sup>c</sup>	20.6 <sup>c</sup>	12.5	9.0	7.5
Male	b	b	b	26.4 <sup>c</sup>	16.9	11.7	10.0
Female	b	b	b	15.1 <sup>c</sup>	8.5	6.6	5.2
Female Genital Organs	30.6	33.4	35.7	34.1	25.8	20.7	15.7
Uterus	b	30.5	29.6	25.2	17.2	12.3	10.7
Breast <sup>3</sup>	19.0	23.9	26.5	27.9	25.2	23.1	21.7
Respiratory System	b	b	5.0	8.6	13.3	20.4	23.9
Male	b	b	7.0	13.3	22.8	36.5	40.6
Female	b	b	2.8	3.9	4.7	6.0	7.7
Trachea, bronchus and lung	b	b	b	6.5	11.7	18.9	22.4
Male	b	b	b	9.7	19.9	34.2	38.2
Female	b	b	b	3.3	4.2	5.6	7.3

<sup>1</sup> The Indirect Method of adjustment was used with United States 1940 rates taken as the standard.<sup>2</sup> Excludes Hodgkin's disease and leukemias.<sup>3</sup> Includes a few male deaths.<sup>a</sup> Excludes pancreas, esophagus and unspecified digestive organs.<sup>b</sup> Deaths are not separately classified.<sup>c</sup> Includes duodenum.<sup>d</sup> Projected civilian population in California 1964 used to calculate rates.

Note: Rates are per 100,000 total, male or female population.

Source: National Office of Vital Statistics: *Vital Statistics of the United States, 1910-40* and unpublished tabulations; U.S. Bureau of the Census: *Vital Statistics Rates of the United States, 1900-40*; California, State Department of Public Health, Death Records.

expectancy), compared with only about one-third of the patients admitted to public hospitals (Table 10). The best experience in cancer of the breast is obtained with women admitted to private hospitals with localized disease—83 per cent five-year relative survival (Table 12). All of these facts suggest that early diagnosis and prompt, adequate treatment may have a significant influence on the outcome of breast cancer. Extending to full application what is now known about the disease might well yield a substantial reduction in mortality.

Mortality from *cancer of the female genital organs* includes principally deaths from cancer affecting the cervix and corpus of the uterus and the ovaries. Cancer of the two major portions of the uterus now accounts for about 1,100 deaths in California each year, and ovarian cancer for almost 750 deaths (Table 1).

However, rapid improvement in the outlook for patients with cancer of the uterus is revealed in survival data given in the Registry. The five-year relative survival in cancer of the cervix (all stages including *in situ*) rose from 40 per cent in 1942-1946 to 63 per cent in 1952-1956 (Table 6). In cancer of the corpus, the corresponding figures were 51 per cent and 67 per cent. A considerable amount of this improvement may be credited to

TABLE 5.—Estimated New Cancer Cases by Site, in California, 1950, 1960, and 1964

Site	1950	1960	1964
All Sites <sup>1</sup>	34,000	53,000	62,000
Lung	1,880	4,670	6,070
Larynx	410	520	580
Stomach	2,640	2,260	2,160
Large intestine	2,600	4,350	4,980
Rectum	1,830	2,520	2,880
Pancreas	760	1,530	1,740
Breast	3,800	5,690	6,620
Cervix uteri <sup>1</sup>	2,050	4,760	6,280
Uterus, other than cervix	1,260	1,750	2,040
Ovary	790	1,340	1,550
Prostate	1,540	3,300	3,700
Kidney	440	780	880
Bladder	1,280	2,300	2,600
Skin, other than melanoma <sup>2</sup>	4,400	5,830	6,760
Leukemia	760	1,550	1,760
All other sites	7,560	9,850	11,400

<sup>1</sup> Includes an estimated 2,610 *in situ* cervical cancer cases in 1960, and 3,770 in 1964.<sup>2</sup> Melanoma of skin included in 1950 estimate.Source: Dorn, H. F., and Cutler, S. J.: *Morbidity from Cancer in the United States*, Washington, 1958 (U.S.P.H.S. Monograph No. 56); U.S. Bureau of the Census: *Census of Population, 1960: California*, Washington, 1962; California, State Department of Finance: *California Population—1963*, Sacramento, 1963; California, State Department of Public Health, California Tumor Registry and Alameda County Registry Records.

widespread use of the cytologic test for cancer (Papanicolaou smear), with consequent early discovery of cancer of the uterus. Some of the improvement may also be attributed to greater use of surgical treatment. Certain additional facts in-

TABLE 6.—Trend in Five-Year Relative Survival Rates, Male and Female Cancer Cases, All Stages Combined,<sup>1</sup> in California, 1942-1956

Site	Five-Year Relative Survival Rate (Per Cent)					
	Male			Female		
	1942-46	1947-51	1952-56	1942-46	1947-51	1952-56
All Sites .....	29.2	36.2	32.9	37.6	47.5	46.9
SELECTED SITES						
Lung .....	2.3	4.5	4.5	4.8	7.4	9.1
Larynx .....	36.6	41.2	46.3	na	na	na
Stomach .....	7.0	10.7	10.1	9.5	13.3	8.8
Large intestine .....	22.3	33.4	33.8	26.1	37.4	40.4
Rectum .....	22.8	31.7	38.0	28.4	36.5	40.1
Pancreas .....	1.4	1.4	1.3	4.0	2.0	2.6
Breast .....	.....	.....	.....	50.5	57.0	57.5
Cervix uteri .....	.....	.....	.....	39.8	54.5	63.2
Corpus uteri .....	.....	.....	.....	50.7	67.1	67.3
Ovary .....	.....	.....	.....	23.8	25.7	23.2
Prostate .....	35.4	37.9	39.4	.....	.....	.....
Kidney .....	22.7	28.3	25.5	30.8	25.6	35.4
Bladder .....	32.6	42.8	48.3	29.9	41.0	42.3
Skin, other than melanoma.....	84.8	89.7	81.9	84.6	94.2	86.5
Leukemia .....	7.1	5.1	6.7	6.4	6.0	5.1

na Not available.

<sup>1</sup> Includes in situ cancer.

Note: Rates were calculated by the actuarial method and have standard errors of less than 10 per cent. Tabulations using year groups 1942-44, 1945-49, 1950-54, and 1955-59 are planned.

Source: California, State Department of Public Health: *Cancer Registration and Survival in California* by the California Tumor Registry, Berkeley, 1963.

TABLE 7.—Trend in Five-Year Relative Survival Rates, Male and Female Cancer Cases, Localized Stage,<sup>1</sup> in California, 1942-1956

Site	Five-Year Relative Survival Rate (Per Cent)					
	Male			Female		
	1942-46	1947-51	1952-56	1942-46	1947-51	1952-56
All Sites .....	62.9	68.8	62.9	66.2	77.8	77.2
SELECTED SITES						
Lung .....	7.6	15.0	15.4	na	32.4	35.9
Larynx .....	na	na	64.5 <sup>a</sup>	na	na	na
Stomach .....	19.9	40.2	37.4	20.3	42.9	32.6
Large intestine .....	na	na	na	na	na	na
Rectum .....	na	na	na	na	na	na
Pancreas .....	2.6	3.8	3.7	0.0	8.7	8.1
Breast .....	.....	.....	.....	75.8	82.7	82.1
Cervix uteri .....	.....	.....	.....	60.0	76.3	85.2
Corpus uteri .....	.....	.....	.....	70.0	84.9	83.0
Ovary .....	.....	.....	.....	62.3	61.1	62.8
Prostate .....	57.0	57.7	56.7	.....	.....	.....
Kidney .....	41.4	51.6	51.0	55.6	46.4	62.1
Bladder .....	46.3	58.8	65.1	43.9	60.2	65.4
Skin, other than melanoma.....	92.9	91.6	84.3	89.8	96.5	88.8
Leukemia .....	.....	.....	.....	.....	.....	.....

na Not available.

<sup>1</sup> Includes in situ cancer.

Note: Rates were calculated by the actuarial method and have standard errors of less than 10 per cent. Tabulations using year groups 1942-44, 1945-49, 1950-54, and 1955-59 are planned.

Source: California, State Department of Public Health: *Cancer Registration and Survival in California* by the California Tumor Registry, Berkeley, 1963.

dicare how much more could be accomplished. In about two-thirds of the patients with cancer of the uterus (corpus and cervix combined) admitted to private hospitals the disease was diagnosed while still in the localized stage when prospects for successful treatment are greatest; by contrast, in only one-third of the patients admitted to public hospitals was the disease diagnosed in the localized

stage (Table 8). The increasing portion of cases of uterine cancer, both corpus and cervix, treated surgically are an indication of the increasing frequency with which these cancers are being diagnosed early in their development. Use of the cytologic test is growing, but it will take organized efforts to achieve greater application of the test especially in those segments of the female popula-



tion at greatest risk of cervical cancer: Negroes and others in poor socio-economic circumstances. The 1952-1956 data indicate that the five-year relative survival rate for localized cancer of the cervix surgically treated was 96 per cent and for localized cancer of the corpus surgically treated 86 per cent.

For *cancer of the ovary*, which now gives rise to more than one-third of all deaths from female genital tract cancer, the outlook is less optimistic than for cancer of the uterus. In California, the five-year relative survival rate continued throughout the 1942-1956 period at about 23 per cent (Table 6). Patients with disease diagnosed in the localized stage showed a 62 per cent five-year relative survival (Table 7). However, the prospects for diagnosing ovarian cancer in the stage when treatment is effective are by no means so good as for cancer of the uterus.

The most common *genital cancer* in males is that of the prostate gland. In 1964, it accounted for about 9 per cent of cancer deaths in California men. Prostate cancer affects principally men in the advanced years of life. While surgical treatment is sometimes feasible and successful, considerable reliance is now being placed on hormonal treatment as a means of relieving symptoms and prolonging life.

*Cancers of the kidney and bladder* are responsible for about 5 per cent of cancer deaths in California (Table 1). Again, the data indicate both improvement in survival during recent years, and potentially greater improvement possible through better diagnosis and treatment (Tables 6 to 11).

*Leukemia* affects over 1,700 persons in California each year but present means of treatment do not afford much basis for optimism. Research on virus and other possible causative factors in several species of animals is now gaining momentum, and several new drugs are being tried.

### Specific Goals and the Means to Reach Them

Goals in the attack on cancer are progress in discovering means of eradication, improving the breadth and quality of services and reducing the mortality from cancer itself.

Measurement of the degree of progress toward discovering means of eradicating the disease as a problem—as has been done in smallpox, pellagra and other conditions—would involve evaluation of accomplishment in research on the cancer prob-

lem, and might best be done nationally since the major research efforts in this field are directed as nationwide activities.

A second way of expressing achievement is to measure the extent of services—educational, medical, social and other services concentrating on the problem. A wide range of medical and related services is needed in each major community of the nation to deal properly with cancer, including: casefinding; definitive diagnosis and treatment; long-term care; and epidemiological-statistical services.

*Casefinding* in cancer depends first of all upon public understanding of and responsiveness to symptoms suggestive of the disease and the need for periodic examinations. The American Cancer Society has played a tremendous part in promoting casefinding; its efforts should be continued and extended. Alert individual medical, dental and paramedical personnel are essential to make the maximum use of present means for detecting cancer in its early stages. They can observe significant signs of disease, and assist the patient to obtain definitive diagnosis and any necessary treatment. In addition, organized casefinding services should be directed specifically to groups of people at greatest risk of cancer. An example is directing the cytologic test for cancer (Papanicolaou smear) particularly to women in low-income segments of the population. Experience, including recent observations in Alameda County, indicate that women at greatest risk are the very ones least likely to obtain appropriate screening, diagnosis and treatment. As general understanding of cancer expands in the community, the importance of identifying target groups—high risk groups—for special casefinding efforts is accentuated.

We are now at the stage when programs for casefinding in cancer, both educational programs and actual services, should be more rigorously organized to focus attention upon those segments of the population most in need—and least responsive to current casefinding techniques. Better organization has helped in the reduction of tuberculosis, has increased immunization against communicable diseases and has aided attacks on other health problems. The time has come to improve casefinding in cancer through better organization.

*Definitive diagnosis and treatment* of cancer constitute an important responsibility of the medical profession. With aging of the population and the consequent relative increase in cancer, physi-

TABLE 8.—Per Cent Cancer Diagnosed in Localized Stage,<sup>1</sup> Male and Female Cases, by Race and by Type of Hospital, in California, 1942-1956

Site	Race				Type of Hospital			
	White		Negro		Public		Private	
	Male	Female	Male	Female	Male	Female	Male	Female
All Sites <sup>2</sup>	47.3	46.8	24.0	33.1	36.4	31.6	52.5	51.5
SELECTED SITES								
Lung	15.1	15.4	8.9	13.2	10.9	9.5	18.1	19.2
Larynx	50.7	58.4	42.3	na	29.3	48.4	62.7	62.2
Stomach	14.6	15.5	9.1	9.6	10.2	8.8	17.2	19.0
Large intestine	na	na	na	na	na	na	na	na
Rectum	na	na	na	na	na	na	na	na
Pancreas	13.2	12.7	6.1	19.6	10.2	9.1	15.3	15.7
Breast	na	40.6	na	25.0	na	25.1	na	43.5
Cervix uteri	na	53.7	na	44.6	na	30.4	na	64.1
Corpus uteri	na	67.4	na	46.3	na	42.7	na	72.3
Ovary	na	26.1	na	21.7	na	13.9	na	29.6
Prostate	51.0	na	32.4	na	34.0	na	61.8	na
Kidney	39.3	44.9	na	44.8	25.2	28.5	45.6	52.4
Skin, other than melanoma	93.6	94.6	80.0	64.1	91.4	91.8	95.2	95.5
Bladder	65.3	61.8	33.8	34.6	40.9	36.4	74.5	70.9

na Not available.

<sup>1</sup> Per cent localized, including in situ cancer, of cases with stage information recorded.

<sup>2</sup> Excludes malignancies of the lymphatic and hematopoietic tissues.

Source: California, State Department of Public Health: *Cancer Registration and Survival in California* by the California Tumor Registry, Berkeley, 1963.

TABLE 9.—Five-Year Relative Survival Rate, Male and Female Cancer Cases, All Stages and Localized,<sup>1</sup> White and Negro, in California 1942-1956

Site	Male				Female			
	All Stages		Localized		All Stages		Localized	
	White	Negro	White	Negro	White	Negro	White	Negro
All Sites	34.2	17.6	65.7	49.2	46.0	34.5	76.0	71.2
SELECTED SITES								
Lung	4.3	5.2	14.9	na	7.9	6.6	30.8	na
Larynx	41.9	na	63.8	na	48.7	na	67.0	na
Stomach	9.8	7.4	34.5	na	10.8	8.6	32.5	na
Large intestine	32.0	25.4	na	na	37.3	29.9	na	na
Rectum	32.2	18.9	na	na	36.9	19.1	na	na
Pancreas	1.3	2.1	2.8	na	2.5	2.1	5.8	9.9
Breast	59.0	na	na	na	56.7	38.5	81.5	73.4
Cervix uteri	na	na	na	na	55.1	48.7	77.0	80.5
Corpus uteri	na	na	na	na	64.7	44.0	82.2	70.0
Ovary	na	na	na	na	27.0	29.2	61.5	78.5
Prostate	38.6	30.8	58.3	51.2	na	na	na	na
Kidney	26.4	22.5	48.8	na	32.4	24.1	58.7	na
Bladder	43.7	8.8	59.7	na	39.8	25.2	59.4	na
Skin, other than melanoma	86.0	85.4	88.9	96.7	90.3	64.4	93.0	92.4
Leukemia	6.2	5.7	na	na	5.7	11.3	na	na

na Not available.

<sup>1</sup> Includes in situ cancer.

Note: Rates were calculated by the actuarial method and have standard errors of less than 10 per cent.

Source: California, Department of Public Health: *Cancer Registration and Survival in California* by the California Tumor Registry, Berkeley, 1963.

cians in general practice and in many specialties will be devoting a greater share of their attention to this group of diseases. Because malignant neoplasms can affect almost any part of the body and be confused with many other conditions, the physician must be constantly alert to the possibility of cancer in his differential diagnosis. A greater proportion of general hospital services is similarly being directed to cancer.

Perhaps the best approach to the problem of

assuring high-quality diagnostic and treatment services for cancer in the hospitals of an urban community is to encourage all general hospitals to develop a good basic cancer service. This would include a tumor board, a cancer registry, and a staff cancer committee to guide these special services as well as to seek opportunities for improving the care of cancer patients by clinical-pathologic conferences and other means. Agreement of the institutions and agencies within a community or



region should then be sought, through areawide planning, to determine which hospitals should develop any needed specialized facilities for the care of cancer patients—for example, by adding new forms of radiation-therapy.

*Long-term care* for cancer patients will be needed on an increasing scale as medical science discloses more and more ways to extend the life—including enjoyable and useful life—of persons with cancer who cannot be cured. This kind of extension of life usually requires close medical supervision, with intensive treatment from time to time. The two major patterns of care for this purpose are nursing home care and home care.

Ideally, it seems desirable to organize long-term care around general hospitals. The medical staff of a hospital could integrate all components of care, assuming responsibility for guiding the quality of nursing home care and home care such as that which now benefits patients in the hospital. This pattern of long-term care appears most likely to promote good medical direction of services through organized medical staff effort directed to maintaining and improving quality of care, and assuring continuity of care between hospital, nursing home and private home. The present isolation of nursing homes from general hospitals and the fragmentary nature of most home care services are leading to greater and greater difficulties in planning good care for long-term patients. Arrangements of services which will be encouraged by the recently passed Medicare legislation should be helpful in this regard. Those concerned with cancer have a particular responsibility to minimize the extent to which long-term cancer patients fall into inappropriate situations and even into the hands of charlatans.

*Epidemiological-statistical services* are receiving more attention in the cancer field as they prove their worth. How far we should go in developing such services remains to be determined. A tumor registry can be especially useful. The purposes of a central tumor registry, as in California, are to:

1. advance epidemiologic knowledge of cancer;
2. evaluate cancer control methods;
3. promote continuing care of the cancer patient; and
4. suggest leads for laboratory and clinical research.

The California Tumor Registry, which compiles and analyzes information from one-third of the

state's hospitals, shows current and needed directions for the entire cancer control effort of the state. Essential to its success are continuous medical guidance, expert statistical direction, the co-operation of hospitals and physicians and adequate resources to collect, process and analyze the data and present reports. Assistance is obtained from the National Cancer Institute, the American Cancer Society and other effective tumor registries.

A third, and perhaps the most appropriate formulation of goals against cancer for California is to project a feasible reduction of the cancer mortality rate based on intensive application of existing knowledge. This reduction would result in part from "primary prevention," that is, the avoidance of occurrence of disease, such as reduction of expected lung cancer deaths by control of cigarette smoking; and in part from "secondary prevention"—the early detection and prompt, adequate treatment of disease, such as further reduction of cervical cancer by systematic application of the cytologic test (Papanicolaou smear) and necessary treatment (Table 13).

## Lung Cancer

At least 75 per cent of deaths now due to lung cancer could be avoided by control of cigarette smoking. Each year beginning about 1970, approximately 3,750 of the 7,500 deaths expected in California from lung cancer could be avoided.<sup>1</sup> One step, the curtailment of cigarette smoking, could reduce the total cancer mortality—about one-sixth within a single decade—that is, by 1975. Elimination of exposure to cigarette smoke would yield not only this benefit; it would also improve health in many other respects, since the use of cigarettes is related to several diseases of the pulmonary system, the cardiovascular system and possibly other parts of the body. From the standpoint of preventive medicine, control of cigarette smoking is one of the most significant measures that could be applied toward improving the health of people in mid-twentieth century America. In California, where cigarette smoking is more common than in the country as a whole, especially among young persons, control is of great urgency.

While a national campaign against cigarette smoking is gradually gaining momentum, a single state such as California can proceed more rapidly. California has taken a strong position on control

<sup>1</sup>Doll, R.: Interpretations of Epidemiologic Data, Cancer Research, 23:10, November 1963.

TABLE 10.—Five-Year Relative Survival Rate, Male and Female Cancer Cases, All Stages and Localized,<sup>1</sup> Public and Private Hospitals, in California, 1942-1956

Site	Male				Female			
	All Stages		Localized		All Stages		Localized	
	Public	Private	Public	Private	Public	Private	Public	Private
All Sites.....	22.7	40.8	54.9	69.9	29.3	51.9	66.8	77.8
SELECTED SITES								
Lung .....	2.1	6.4	4.4	20.1	3.8	11.2	na	38.8
Larynx .....	21.4	56.1	42.0	70.5	39.1	51.2	na	na
Stomach .....	5.7	12.9	23.0	39.8	7.2	13.1	20.4	37.3
Large intestine .....	17.4	38.2	na	na	21.8	43.0	na	na
Rectum .....	16.5	40.2	na	na	19.4	43.0	na	na
Pancreas .....	0.9	1.7	2.2	4.0	0.8	3.9	5.7	7.4
Breast .....	30.1	68.3	na	na	34.7	61.5	67.4	83.1
Cervix uteri .....	na	na	na	na	39.0	62.5	78.0	77.0
Corpus uteri .....	na	na	na	na	42.2	69.8	71.8	83.1
Ovary .....	na	na	na	na	17.7	26.5	61.4	62.6
Prostate .....	29.1	45.9	50.0	60.1	na	na	na	na
Kidney .....	12.5	33.5	30.8	54.0	16.5	38.0	39.6	60.3
Bladder .....	22.7	52.3	38.2	63.5	18.7	49.7	45.0	62.0
Skin, other than melanoma.....	74.3	94.7	77.1	97.3	79.5	95.5	82.5	98.1
Leukemia .....	3.9	8.0	na	na	4.9	6.8	na	na

na Not available.

<sup>1</sup> Includes in situ cancer.

Note: Rates were calculated by the actuarial method and have standard errors of less than 10 per cent.

Source: California, State Department of Public Health: *Cancer Registration and Survival in California* by the California Tumor Registry, Berkeley, 1963.

of cigarette smoking, through the efforts of the Interagency Council on Cigarette Smoking and Health and the Governor's Advisory Committee on Smoking and Health, and by interests of legislators, physicians, health agencies and educators. But these efforts—and action—take time to affect human behavior. They must be doubled and trebled in the immediate years ahead.

Clearly, the reduction of cigarette smoking can save thousands of deaths from lung cancer. This known form of primary prevention offers the most optimistic goal—in terms of sheer numbers of lives saved—if applied fully and swiftly.

## Gastrointestinal Cancer

Cancer of the stomach is declining although medical scientists are not certain why. Survival of patients with cancer of the stomach could probably be improved somewhat through greater attention to early diagnosis and treatment. However, the nature of its manifestations and the limited effectiveness of current means for dealing with it do not offer much basis for setting a realistic goal. Something may yet be found to accelerate the present decline of stomach cancer which in California still results in approximately 1,600 deaths each year.

On the other hand, the situation with respect to cancer of the large bowel and rectum does provide a basis for some optimism. At present approximately two-fifths of patients with these forms

TABLE 11.—Per Cent Localized\* Cancer Cases by Sex and Time Period, in California, 1942-1956

Site	1942-46	1947-51	1952-56
<i>Both Sexes</i>			
All Sites, <sup>1</sup> Excluding Skin.....	35.2	39.3	41.1
Accessible sites, excluding skin..	41.4	47.4	51.6
Inaccessible sites.....	29.7	32.6	33.1
<i>Male</i>			
All Sites, <sup>1</sup> Excluding Skin.....	34.2	37.0	37.4
Accessible sites, excluding skin..	46.0	51.2	53.9
Inaccessible sites.....	28.0	30.3	30.2
<i>Female</i>			
All Sites, <sup>1</sup> Excluding Skin.....	35.9	41.0	44.0
Accessible sites, excluding skin..	39.3	45.7	50.6
Inaccessible sites.....	31.5	35.3	36.6

\* Includes in situ.

<sup>1</sup> Excludes malignancies of the lymphatic and hematopoietic tissues.

Note: Tabulations using the year groups 1942-44, 1945-49, 1950-54, 1955-59, and 1960-62 are planned.

Source: California, State Department of Public Health: *Cancer Registration and Survival in California* by the California Tumor Registry, Berkeley, 1963.

of cancer survive at least as long as five years. Considering the improvement in survival during the past couple of decades, the better prognosis if the disease is discovered in the localized stage and the more favorable outlook for patients receiving private care than for those receiving public care, it would appear that further improvement in survival would be a reasonable goal, such as a relative survival rate of about 50 per cent, rather than 40 per cent. This would mean a reduction of about 800 each year beginning in 1970 from the approximately 4,000 deaths expected as a result of cancer of these sites. With intensive effort this goal might be exceeded.



In order to achieve or exceed this goal for reduction of mortality from cancer of the colon and rectum, two elements are essential: (1) greater public education concerning the significance of signs and symptoms of abnormality of the lower gastrointestinal tract, particularly change in bowel habits or in the appearance of the stool, and bleeding; and (2) elevation of the level of cancer-suspicion by practicing physicians who can observe abnormalities and can encourage thorough examinations when these symptoms occur. Some physicians still tend to attribute rectal symptoms to hemorrhoids when, in fact, cancer may be present.

One means of accomplishing professional education, as well as acquiring greater insight into the problem, would be to review every death from cancer of the rectum in the same way that maternal deaths have been investigated for many years—cooperatively by the medical profession and health departments. Systematic review of maternal deaths by panels of experts, to determine those factors leading to maternal deaths, has tremendously increased our understanding of deficiencies, both of expectant mothers and their physicians. These reviews have had a salutary effect on obstetric practice, and are generally regarded as having contributed to the great reduction in maternal mortality during recent decades.

The situation with respect to cancer of the rectum, cancer of the cervix and of certain other sites where treatment can be highly effective, seems to offer similar promise. The medical society could collaborate with the health department in referring every death from one or two particular sites of cancer, for example, rectum or cervix, for which diagnosis and treatment are effective, to an expert panel for review. Limiting the attention to one or two sites would keep the work from becoming excessive.

As in the case of maternal death reviews, the panel would investigate details of patient care, including patient and physician factors. Data could be compiled from such reviews, indicating specific aspects of public and physician education which need further attention. The procedure would no doubt also enhance patient care, through physician awareness of the review procedure—again as occurred in maternal death studies.

## Breast Cancer

By 1970, present trends indicate that cancer of the breast will be causing about 2,700 deaths an-

nually in California. Continuing decline in the mortality rate from breast cancer during recent decades and other aspects of the picture provide a basis for even greater reduction. As was previously noted, there appear to be several grounds for seeking improvement: increase in relative survival rate, both for localized disease and all stages combined; better survival experience with localized disease; and more favorable outcome in private hospitals than in public hospitals. Perhaps it would be reasonable to establish a modest goal—a mortality reduction of about one-fifth, that is, 600 deaths each year from the 2,700 anticipated. To accomplish this will require intensification of educational efforts and the use of all available useful techniques for the diagnosis and treatment of breast cancer—among all women in the population affected.

## Female Genital Tract Cancer

Cancer of the uterus, cervix and corpus combined continues to result in about 1,100 deaths annually in California. The decline in the mortality rate due to more effective medical care is practically compensated by the increase in population and in the proportion of the aging. Many signs indicate that the toll could be reduced substantially: the mortality rate has been dropping; the five-year relative survival rate has increased substantially, both for localized disease and all stages combined; more cases are being diagnosed in the localized stage; patients in private hospitals have better experience than patients in public hospitals.

The problem in cancer of the uterus may be illustrated by experience with the cytologic test for cancer of the cervix (Papanicolaou smear). In Alameda County—a region quite typical of the state as a whole (urban, relatively high proportion of Negroes, progressive medical community)—a survey disclosed in 1962 that about half the women had received a cytologic test at least once. However, the extent ranged from two-thirds among the native-born white women in the upper social classes to only one-fourth among the Negro and foreign-born women at the lower end of the socio-economic scale. Thus, the very group of women with the greatest incidence of the disease, as shown by extensive mortality and morbidity data, are least likely to receive the benefits of the most effective means for dealing with it. Three of the most influential factors in obtaining the test were knowledge of the existence of the test, advice of physicians and having a health in-

TABLE 12.—Trend in Per Cent Localized Female Breast Cancer Cases by Race and by Type of Hospital, in California, 1942-1959

	Total Number				Per Cent Localized			
	1942-44	1945-49	1950-54	1955-59	1942-44	1945-49	1950-54	1955-59
All Cases .....	1,558	3,716	5,416	6,808	36.3	37.5	41.3	44.2
White .....	1,451	3,525	5,200	6,411	36.9	37.9	42.0	44.7
Negro .....	45	139	228	347	13.3	25.9	24.1	34.6
Public hospitals.....	289	289	1,013	1,365	12.5	21.2	28.0	37.3
Private hospitals.....	1,269	3,007	4,448	5,443	41.7	41.3	44.3	45.9

Source: California, State Department of Public Health, California Tumor Registry data on breast cancer presented at the Fifth National Cancer Conference by L. Breslow.

surance or medical prepayment plan—particularly a comprehensive prepayment plan.

With intensive effort, it would seem possible to effect a reduction of 850 uterine cancer deaths, cervix and corpus combined, from the approximately 1,100 expected during the early 1970's in California. This would require acceleration of the present program to find cases early and bring them to treatment, and especially directing specific efforts toward those segments of the population at greatest risk.

Cancer of the ovary is an increasing component in female cancer mortality, but experience in dealing with it unfortunately does not justify setting a large achievement as a goal. It is true that patients receiving private care tend to have the disease diagnosed in a localized stage to a greater extent (Table 8) and to have a better five-year relative survival (Table 10). This may be sufficient to establish as a goal a reduction of 150 deaths from the approximately 900 expected from cancer of the ovary in California during the early 1970's.

### Male Genital Tract Cancer

Cancer of the prostate gland is causing increasing mortality as more men live beyond "three-score years and ten." The fact that there has been only a modest improvement in five-year relative survival rate for all stages combined (Table 6) and no improvement in the localized stage (Table 7) suggests that a modest goal is indicated. The 50 per cent better experience in private care compared with care under public auspices (Table 10) does offer a rationale for seeking improvement. Reducing by 150 the anticipated 1,300 deaths each year from prostate cancer in California, beginning about 1970, would seem a reasonable aim.

### Cancer of the Kidney and Bladder

Experience with cancer of the kidney and bladder in many respects typifies what is occurring and what may be expected from medical care in the control of cancer (Tables 6 to 11). While these

TABLE 13.—Annual Cancer Deaths Expected in California During Early 1970's (Based on 1950-1960 Trend)

Site	Number Deaths Expected
All Sites .....	30,000
Lung .....	7,500
Stomach .....	1,600
Colon and rectum.....	4,000
Pancreas .....	1,800
Breast .....	2,700
Uterus .....	1,100
Ovary .....	900
Prostate .....	1,300
Kidney and bladder.....	1,400
Leukemia .....	1,700
All other sites.....	6,000

Source: California, State Department of Public Health, Death Records; California, State Department of Finance: *California Population—1963*, Sacramento, 1963.

sites are not common—together they account for about 5 per cent of cancer mortality—they are one more focus for attack. Progress is being made as measured by five-year relative survival, both for all stages combined and for localized cancer. Along with other data, this fact probably warrants setting as a proper goal reduction by 400 of the expected 1,400 deaths from cancer of these sites during the early 1970's in California.

### Leukemia

Because this form of cancer affects the very young as well as the old, it would be particularly stimulating to specify a goal based on current knowledge. Unhappily, while some extension of life is being achieved through chemotherapy and other treatment, the major focus in this disease must remain on research. Each year many new drugs are tried and some appear sufficiently promising to justify sustaining strong research and clinical efforts. Most exciting at the moment is the possibility of identifying a virus which causes human leukemia, as has been demonstrated in other species, and the possibility of controlling the disease through this knowledge.

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# Diagnosis of Brain Tumors

## A Comparison of Photoscanning and Neuroradiological Techniques

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■ *Results of radioisotope photoscans and diagnostic neuroradiological procedures performed in 167 patients with suspected brain tumors led to the conclusion that correct identification of the intracranial process can be obtained in a high proportion of cases by the proper selection of available diagnostic techniques. The radioisotope photoscan had a relative diagnostic accuracy nearly equal to that of the neuroradiological techniques. The accuracy, taken with the relative ease and safety of the method, make it an ideal screening procedure in cases in which intracranial pathologic change is suspected.*

CEREBRAL ANGIOGRAPHY, pneumoencephalography and ventriculography have been used for many years for further investigation when brain tumor is suspected clinically. More recently, various radioisotopes have been utilized in the diagnosis and in determining the location of intracranial lesions.<sup>2,3,9,12,15</sup> The isotope procedures have been particularly stressed as screening procedures.<sup>7,13,16</sup> Various isotope techniques have been employed successfully in localizing brain tumors.\*

In an attempt to assess the value of radioisotopic brain scans, the results of brain scanning were compared with results of various neuroradiological procedures. The records of 167 patients who had isotopic brain scans and either cerebral angiography or encephalography, were reviewed. These patients were seen at the University of California Hospitals, San Francisco, in the period July 1962 through March 1964. In each case the original interpretations of these various studies

were compared with each other and with the final diagnosis.

The selection of the initial diagnostic roentgenologic procedure for each patient was determined by the clinical information. Cerebral arteriography was performed in 48 patients, encephalography in 38 and a combination of angiography and air-contrast study in 81.

An intravenous dosage of <sup>203</sup>Hg-chlormerodrin, 8 to 10 microcuries per kilogram of body weight, was given in all but two cases. The scanning procedure, utilizing a Picker Magna Scanner and photoscanning, was usually started four hours after intravenous administration of the radioisotope. A lateral and an anterior or posterior scan was obtained in each study. Additional scans were obtained in selected cases.

### Results

The results of the various diagnostic procedures were interpreted as demonstrating the presence or absence of, or as being suggestive of, findings consistent with a brain tumor. Histologic proof was

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\*Reference Nos. 1, 3, 4, 9, 17.

available in 85 patients. In the other 82 patients no pathologic material was available and the diagnosis at time of discharge was accepted and utilized in the tabulation. Any difference between the interpretation of the angiographic, air-contrast and radioisotopic procedures was considered a disagreement. A difference in localization of tumor site or in the number of recognized lesions was also considered an instance of disagreement. In this analysis, complete agreement among the various techniques was found in only 98 (59 per cent) of the 167 cases.

Patients in this series were separated into "non-tumor" and "tumor" groups on the basis of the final diagnosis.

*Nontumor groups.* Cerebral abnormality other than intracranial tumor was the final diagnosis in 86 patients. In 61 of these patients, no sign of tumor was found by any technique. Included were 15 patients with a final diagnosis of cerebrovascular insufficiency. In eight cases, at least one of the roentgenologic results suggested a space-occupying lesion, but the scans were negative. The roentgen studies in an additional eight patients were negative, but the photoscan, which suggested increased radioactivity in one view, was not confirmed in the accompanying view. In three patients a benign cystic lesion was found. In one of the three an arachnoid cyst of the inferior frontal lobe was diagnosed on carotid arteriography as a mass in the temporal lobe. It was not identified on the pneumoencephalogram or on the photoscan. In the second patient a congenital cyst of the occipital lobe was diagnosed as a space-occupying lesion on both pneumoencephalogram and carotid ar-

teriogram. This lesion was not demonstrated on the photoscan. A mass in the cerebellopontine angle observed at encephalography of the third patient proved to be an extradural cyst, possibly a cholesteatoma. The photoscan of this patient, in the lateral projection only, suggested localization in the anterior cerebellar region.

In three patients with an angiographic diagnosis of intracranial hemorrhage or cerebrovascular occlusion, the photoscans showed concentration of radioactivity in the area of the vascular accident.

In another patient, surgically proved basilar arachnoiditis had been interpreted at ventriculography as a suprasellar tumor. The results of bilateral carotid arteriograms and photoscans were normal.

An abscess of the frontal lobe was correctly localized by both arteriography and photoscan.

Bilateral carotid arteriograms of an additional patient were reported as showing no abnormalities, but a faintly positive localization was seen in the parasagittal region of both views of the photoscan. The diagnosis at the time of discharge was diffuse disease of the central nervous system, possibly vascular in origin. The photoscan in this instance was interpreted as showing a tumor and must be considered as a false positive interpretation.

*Tumor cases.* A primary or metastatic tumor of the brain was diagnosed in 81 of the 167 patients. Histologic proof was available in 65 of the 81. The various types of tumor found and the number of cases in which the presence of tumor was shown by each procedure are shown in Table 1. A discussion of the agreement or disagreement among

TABLE 1.—Positive Identification of Brain Tumors by Photoscanning and Neuroradiological Techniques

Tumor type	Number of cases	Angiography		Pneumo-encephalography		Isotope photoscan		Complete agreement among procedures	
		Number correct	Number studied	Number correct	Number studied	Number correct	Number studied		
Astrocytoma .....	19	16	16	15	16	9	19	8	19
Glioma and glioblastoma .....	14	10	14	4	5	14	14	10	14
Oligodendroglioma .....	3	2	2	1	1	2	3	2	3
Medulloblastoma.....	1	----	----	1	1	0	1	0	1
Ependymomas .....	2	----	----	2	2	2	2	2	2
Meningioma .....	12	9	11	5	6	11	12	9	12
Meningeal sarcoma .....	2	0	1	1	2	0	2	0	2
Cerebellopontine angle....	3	0	0	2	3	0	3	0	3
Pituitary tumors .....	3	2	2	2	3	3	3	2	3
Metastatic tumors .....	14	9	14	7	8	12	14	5	14
Inoperable tumors .....	4	4	4	4	4	2	4	2	4
Tumor suspect .....	1	0	1	1	1	0	1	0	1
Died without necropsy....	3	2	3	2	3	1	3	1	3
TOTAL .....	81	54	68	47	55	56	81	41	81
		(79 per cent)		(85 per cent)		(69 per cent)			



the diagnostic procedures for each tumor type follows:

*Astrocytoma.* Complete agreement in the diagnosis was obtained by means of roentgen and radioisotope procedures in eight of 19 tumors in this category. In one patient, a tumor that was suspected on a technically unsatisfactory pneumoencephalogram as being in the right frontal area was verified by positive photostan. In four patients, photostans were suggestive of but did not positively identify tumors that had been diagnosed correctly by pneumoencephalography or arteriography. Well differentiated frontal lobe astrocytomas diagnosed roentgenologically in three patients were not identified by the photostan. Identification of a fibrillary astrocytoma of the frontal lobe in another patient was positive on the angiogram but not confirmed by pneumoencephalogram or photostan.

In one patient a grade III astrocytoma of the thalamus, correctly identified by both pneumographic and angiographic studies, was not identified by the photostan. A large calcified subependymal astrocytoma in the third ventricle was diagnosed by angiography and pneumoencephalography but on the photostan the site was not positively localized.

*Glioma and Glioblastomas.* All 14 lesions in this category were correctly localized by photostan. Arteriographic and air-study, however, were correct in only 10 instances. One lesion was missed at arteriography because of technical problems. In another patient, a cystic glioma of the parietal lobe was suspected, but not definitely diagnosed, on a carotid arteriogram. Angiographic differentiation between postoperative changes and recurrence was not possible in one patient with a recurrent lesion in the temporal lobe. Carotid arteriograms repeated three months later showed a definite recurrence of tumor. Arteriograms and pneumoencephalograms were considered normal in a patient with a lesion of the frontal lobe that was distinctly positive on the photostan. Roentgen studies repeated one month later, however, showed the presence of a frontal lobe glioblastoma.

*Oligodendrogliomas.* Postoperative recurrences were correctly identified by arteriography and photostan in one patient and by pneumoencephalogram and photostan in another. In a third patient, a partly calcified frontal lobe tumor was positively identified by arteriogram but only suspected on the photostan.

*Medulloblastoma.* A medulloblastoma filling the fourth ventricle was correctly diagnosed at ventriculography, but was not identified by a photostan.

*Ependymoma.* The two ependymomas in this series were correctly identified by both ventriculography and photostan.

*Meningiomas.* The methods were in complete agreement as to localization in nine of the 12 cases of meningiomas. A recurrent meningotheelial meningioma of the tuberculum sellae was not identified by the photostan technique, but was identified by both angiographic and pneumographic studies. Recurrence of a large lesion of the occipital lobe in another patient was suggested by angiographic studies and demonstrated by scan. A sphenoid-wing meningioma identified subsequently by photostan had been suspected by angiographic studies, but not identified on pneumoencephalography.

*Meningeal sarcoma.* In one patient, diffuse meningeal sarcomatosis was suspected on the basis of pneumoencephalography but was not noted on photostan. A second patient had a parasagittal subdural lymphosarcoma identified on pneumoencephalography but not seen on angiogram and only suspected on photostan.

*Cerebellopontine angle tumors.* Incomplete pneumoencephalograms and a photostan did not identify an acoustic neurinoma in one patient. Plain roentgenograms of the skull, however, showed erosion of the internal auditory meatus. In two additional patients with acoustic neurinoma the lesions were identified by pneumoencephalography, but photostans were negative in one and only suggestive in the other.

*Pituitary tumors.* One recurrent suprasellar extension of a chromophobe adenoma and one craniopharyngioma were correctly identified by all three techniques. In another case in which recurrence was suspected on pneumoencephalography but not confirmed by photostan, only scar tissue was found on surgical operation.

*Metastatic tumors.* Biopsy of the primary tumor was available in each of the 14 instances; in only six, however, was the suspected metastatic cerebral focus histologically confirmed. Complete agreement as to the site and number of metastatic lesions was noted in five instances. In two patients, multiple lesions were reported on photostan, but

only single lesions were observed at angiography. In another patient, only one lesion was observed on the scan, whereas two were found on angiography. Single metastatic lesions in three other patients, positively identified by photoscan, were only suggested at angiography; a pneumoencephalogram, however, confirmed the diagnosis in one of these patients. One metastatic tumor was identified on photoscan but not on angiograms. In two patients, a single metastatic lesion was identified by pneumoencephalography and arteriography, but on photoscan was only suspected in one patient and not observed at all in the other.

*Inoperable tumors.* In four patients, histologic confirmation of suspected tumor could not be obtained, as the location of the tumor made biopsy excessively hazardous. A mass in the lateral ventricle in one patient and a cystic tumor of the thalamus in another were positively identified by all three techniques. A probable pinealoma and a tumor anterior to the pons, missed by photoscan, were diagnosed by angiography and pneumoencephalography.

*Suspected tumor.* One patient with a suspected brain tumor was included in the series. Identification was positive in the parasagittal area on pneumoencephalography, suggestive on photoscan and not confirmed on arteriograms. The patient died three months later in another hospital. The death certificate stated that an uncus herniation secondary to glioblastoma multiforme caused death.

Postmortem confirmation was not obtained in three patients in whom brain tumor was suspected.

## Discussion

A comparison of the accuracy of pneumoencephalography, arteriography and photoscan techniques in the diagnosis and localization of brain tumors is difficult. Our series was limited to patients who had had both a brain photoscan and an arteriogram or encephalogram. The use of isotopic techniques in addition to the standard neuro-radiologic procedures was often determined by the need for additional information in doubtful or difficult diagnostic problems. The selection of patients in this series is, therefore, a necessarily biased one, and the true accuracy of the various available techniques is difficult to assess.

Arteriographic diagnosis was accurate in 54 of 68 tumors in this series (79 per cent). In an additional six patients (9 per cent), the correct diag-

nosis was suspected on angiography and was confirmed by either encephalography or photoscan.

Pneumoencephalography or ventriculography provided a correct diagnosis in 47 of 55 cases of intracranial tumor (85 per cent). In three additional patients, tumors were suspected on pneumoencephalography and the diagnosis was confirmed by the other techniques, raising the accuracy to 91 per cent.

Of the 81 patients with intracranial tumors, the photoscan was reported as positive in 56 (69 per cent). Localization which had been suspected in both views in an additional nine patients was confirmed by the other procedures, making the accuracy of the combined technique 80 per cent.

Only one of the tumors in this series, an acoustic neurinoma, was missed by pneumoencephalographic examination and isotope photoscan. False positive localization was reported in one pneumoencephalographic study and in one isotope photoscan.

Positive localization with a photoscan technique depends on a breakdown in the normal blood-brain barrier. Any condition that alters this normal barrier can produce the evidence for a positive localization.<sup>4-6,11,18</sup> Localization in this series was positive, therefore, not only in tumors, but also in acute abscess, vascular occlusion and recent intracerebral hemorrhage. The radioactivity in the cases of cerebral vascular accident was not, however, as concentrated as that generally noted in localization of primary and metastatic tumors.

Difficulties in localizing cystic slow-growing tumors by using isotope techniques have been reported.<sup>8,19</sup> Tumors of this type, present in nine of the cases in the present series, were not positively identified by photoscan. Difficulties have also been reported in the isotope localization of tumors near the midline, in the posterior fossa and adjacent to the base of the skull where vascular background activity is high.<sup>4,10,14,19</sup> Ten tumors not localized by photoscan techniques in the present series were at these adverse locations.

The accuracy of results of radioisotope techniques in relation to tumor type has been reported previously.<sup>11,13,14,18,19</sup> Similar results were obtained in this series. On several occasions the distinctly positive localization prompted surgical intervention when results of roentgen procedures were only suggestive or were negative. Distinct localization on isotope photoscan has also been used to direct the placement of ports for radiation therapy in in-



stances of known tumor recurrence, thus avoiding the need for surgical reexploration.

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# Privileged Communications

## *The Effect of California's New Evidence Code As It Concerns Physicians and Psychotherapists*

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■ *A physician has an ethical duty to hold in confidence communications made to him by his patient. A legal recognition of this ethical duty is found in the concept of privilege, which is the subject of this article. January 1967 will bring to California physicians a new protection for patients' communications. The physician-patient privilege has been redefined to include confidential communications made during diagnostic evaluation, those made to non-licensed physicians, interns and medical aides, and those overheard by eavesdroppers. There has been added a psychotherapist-patient privilege designed to facilitate communications required in psychotherapy as well as in behavioral research.*

*This paper first presents a brief historical background and discusses the protections and limitations afforded by the new California Evidence Code. There follows a section on the psychotherapist-patient privilege with the recommendation that in the context of psychotherapy, patients of physicians who are not psychiatrists should be afforded the additional benefits of the psychotherapist-patient privilege. Lastly, advice is given concerning the physician's conduct in relation to his duty to claim privilege under the new code.*

THE ETHIC OF CONFIDENTIALITY is clearly voiced in the Oath of Hippocrates,<sup>8</sup> which marked its earliest recognition in the medical tradition of Western Civilization. This oath, in part, states, "And whatsoever I shall see or hear in the course of my profession, as well as outside my profession in my intercourse with men; if it be what should

not be published abroad, I will never divulge, holding such things to be holy secrets." Thus is expressed a broad ethic of confidentiality that includes not only the verbal content of whatever is divulged, but also the "personality" of the patient and his environment.

In modern continental Europe, and particularly in France and Germany, the confidentiality of the transactions occurring between the physician and his patient have been accorded a broad protection.<sup>7</sup> Each of these countries includes in its

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laws express provisions affording this protection. In contrast, the English tradition<sup>15</sup> grants no express statutory provision regarding privilege although barristers and judges at times handle the matter of confidentiality under a concept of "fundamental fairness." This means that communications occurring in socially significant relationships, such as those of lawyer-client,<sup>14</sup> clergyman-parishioner,<sup>10</sup> and physician-patient may be protected against disclosure, depending upon the demands of the circumstances.

New York, in 1828, was first in the United States to enact a statute recognizing the ethic of confidentiality in the physician-patient relationship.<sup>13</sup> So few states followed that California, when it recognized this ethic in a legislative manner<sup>16</sup> in 1872, was still among only a handful that had done so. The 1872 California statute<sup>4</sup> exists today in substantially the same form as when it was first enacted. Developments under this statute have been comprehensively reviewed by Hassard.<sup>12</sup>

The deficiencies of the existing privilege statute include a failure to cover within its provisions (1) non-licensed medical personnel such as interns, (2) physician's helpers, such as nurses, secretaries and social workers, and (3) eavesdroppers. Further it fails to cover the physician's diagnostic workup if treatment does not ensue. Until recently, patients of psychiatrists have had no particular protection other than the physician-patient privilege, although since 1957 a certified psychologist has been able to accord his patient protection commensurate with the broad attorney-client privilege.<sup>3</sup>

The ethic of confidentiality permeates all activities of the physician. For breach of this ethic a physician may be subject to disciplinary proceedings that could result in loss of license to practice.<sup>2</sup> He may also incur civil liability to his patient for willful disclosure of confidential information<sup>9,12</sup>; in such a situation the physician will not be judged by his own professional peers, but by a jury of laymen. In certain circumstances, however, disclosure of confidential information regarding a patient may be required, as elaborated below.

## Medical Privileges of the New Code

For purposes of quick reference and in view of its brevity, the appropriate sections of the new Evidence Code<sup>5</sup> concerning (1) physician-patient privilege and (2) psychotherapist-patient privilege

which will go into effect in January 1967 are presented in their entirety. This is done in parallel columns (printed at the end of this article as Appendix) to facilitate handy cross comparison between the items governing physician-patient and those governing psychotherapist-patient privilege.

## Scope of the Medical Privileges

For the physician-patient privilege to be applicable in a proceeding, three requisites<sup>1</sup> must be satisfied: (1) The physician-patient relationship must have been established; (2) the communication under inquiry must have been an outcome of that relationship and not merely an outgrowth of a social encounter; and (3) the communication must have been made under confidential circumstances.

The physician-patient relationship has its analogue in a contract<sup>7</sup> for personal services wherein confidentiality is an implied condition.<sup>9,15</sup> It should be understood that the patient is the owner of the privilege, not the physician. The physician, however, has a legal duty under the new code (Section 995) to claim the privilege for the patient. This duty arises in *any* situation when the physician may be subpoenaed.

Several major deficiencies of the current statute will be corrected by the new Evidence Code. Confidential communications to non-licensed physicians, including interns, will be covered as well as those transmitted through medical aides; confidential communications during a diagnostic workup (including a single visit) will be protected; and confidential communications overheard by eavesdroppers will be excluded from disclosure in legal proceedings.<sup>5</sup>

Physicians often ask whether consultation or review of a case by a hospital tissue or records committee destroys the confidentiality of the record. It has always been the opinion of the general counsel of the California Medical Association that it did not.<sup>11</sup> This point of view is now made explicit by the California Legislature in a comment on the new code<sup>5</sup>: "Nor would a physician's or psychotherapist's keeping of confidential records necessary to diagnose or treat a patient, such as confidential hospital records, be a waiver of privilege, even though other authorized persons have access to the records . . . because such disclosure is reasonably necessary for the accomplishment of the purpose for which the physician is consulted."

## Exceptions to the Medical Privileges

The physician-patient privilege will be denied and disclosure of information compelled in legal proceedings wherein the patient's criminal behavior is an issue. Another exception to the privilege is the situation in which the patient himself is a party to a lawsuit and has tendered his physical, mental or emotional condition as an issue. In effect, this is a waiver of the privilege. In controversies arising from the physician-patient relationship such as suits for malpractice or actions for the fee, the privilege does not apply. Where a patient's mental capacity to execute a deed or a will is an issue, the privilege does not apply, and disclosure by the physician may be compelled. There is also no physician-patient privilege in a disciplinary proceeding such as to revoke or suspend a physician's license.

## The Psychotherapist-Patient Privilege

In addition to the physician-patient privilege, there will soon be expressly recognized in the California statutes a psychotherapist-patient privilege. Previously, a psychiatrist could afford his patients protection of a communication only under the physician-patient code section. It was evident to the framers of the new privilege sections that effective psychotherapy demanded a broader privilege which would not deter the fullest revelation of the most intimate and potentially embarrassing details of the patient's life.<sup>5</sup> In modern psychotherapy, it is recognized that full disclosure is a keystone in the structure of treatment. Therefore, protection was extended even to communications involving criminal behavior, in recognition of the position that in the long run society would benefit even though an occasional act of criminal behavior might go unredressed. Hence, the psychotherapist privilege extends beyond the physician-patient privilege in that it applies to an area of criminal activity. Further, the California psychotherapist-patient privilege gives recognition and encouragement to behavioral research by protecting communications of subjects.

A major deficiency of the new psychotherapist-patient privilege is that it does not recognize the legitimate and necessary requirements of patients whose physician may not devote "a substantial portion of his time to practice of psychiatry," but who are treated by that physician through psycho-

therapy—a tool that demands protection of communications.

Most persons who take their problems to physicians go first to their personal physician, be he generalist or specialist. It is in the context of that relationship and possibly even in the first visit, that the patient "spills his guts" relative to an emotional or mental problem. This physician may treat the patient for his emotional problems, using tools very similar if not identical to those used by a psychiatrist, including supportive psychotherapy. He may or may not refer the patient to a physician designated as a psychiatrist. In either event, it is in the patient's best interest from the point of view of diagnosis and treatment that his confidential communications be protected so as to encourage full disclosure to the physician of his mental and emotional problems. This important point was made initially by the framers of the new privilege section,<sup>6</sup> but was lost during subsequent drafts. To do justice to the patient who is receiving psychotherapy from a non-psychiatrist, as described above, we recommend to the California Legislature the following addition to Section 1010:

*1010 (c)—A physician within the meaning of Section 990 who treats the patient in a manner substantially similar to the treatment that would be rendered by a person within the meaning of Section 1010 (a).*

## Advice to the Physician

In view of the duty of the physician or psychotherapist under the New Code to claim the privilege, the claim should be made at each opportunity. A first opportunity would be when the physician or psychotherapist is served with a subpoena requesting his attendance at a deposition or hearing. A simple procedure at this time may consist of a telephone contact with the attorney whose name appears on the subpoena and a statement to him that the information regarding the patient is privileged. If the attorney is unwilling to vacate the subpoena the physician must appear as specified.

The next situation in which the privilege is to be claimed is when the physician's deposition is being taken or when he is testifying in court, before a grand jury, or before a legislative or administrative committee. When a question is posed regarding communications made by a patient to him, the physician should suggest to counsel or to the pre-



siding officer that such information is privileged. This will give counsel or the presiding officer an opportunity to state for the record whether or not the physician must answer the question.

Under no circumstances should a physician disclose a patient's records, x-ray films or any other data to an attorney until the physician has been assured that the patient has waived confidentiality. If the physician is certain that he is dealing with the patient's attorney, he can accept the attorney's word and then release the information without fear of liability, although the physician may also request a consent signed by the patient. When dealing with the attorney of the patient's adversary, which is not infrequently the case, no steps should be taken by the physician until the patient's attorney has been contacted. The patient's attorney should advise the physician regarding disclosure of information and records.

Little by little, law catches up with the needs of the community regarding good medical practice. A great stride has been taken by the 1965 California Legislature to enable more effectual care of patients by expanding the concept of medical privilege. But to come more fully abreast with current scientific knowledge, as it relates to psychotherapy, we believe that the need for broader protection of patient-physician confidentiality must be legally recognized.

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## APPENDIX

### PHYSICIAN-PATIENT

#### ARTICLE 6.—*Physician-patient Privilege*

990. As used in this article, "physician" means a person authorized, or reasonably believed by the patient to be authorized, to practice medicine in any state or nation.

991. As used in this article, "patient" means a person who consults a physician or submits to an examination by a physician for the purpose of securing a diagnosis or preventive, palliative, or curative treatment of his physical or mental or emotional condition.

### PSYCHOTHERAPIST-PATIENT

#### ARTICLE 7.—*Psychotherapist-patient Privilege*

1010. As used in this article, "psychotherapist" means:

(a) A person authorized, or reasonably believed by the patient to be authorized, to practice medicine in any state or nation who devotes, or is reasonably believed by the patient to devote, a substantial portion of his time to the practice of psychiatry; or

(b) A person certified as a psychologist under Chapter 6.6 (commencing with Section 2900) of Division 2 of the Business and Professions Code.

1011. As used in this article, "patient" means a person who consults a psychotherapist or submits to an examination by a psychotherapist for the purpose of securing a diagnosis or preventive, palliative, or curative treatment of his mental or emotional condition or who submits to an examination of his mental or emotional condition for the purpose of scientific research on mental or emotional problems.

992. As used in this article, "confidential communication between patient and physician" means information, including information obtained by an examination of the patient, transmitted between a patient and his physician in the course of that relationship and in confidence by a means which, so far as the patient is aware, discloses the information to no third persons other than those who are present to further the interest of the patient in the consultation or those to whom disclosure is reasonably necessary for the transmission of the information or the accomplishment of the purpose for which the physician is consulted, and includes advice given by the physician in the course of that relationship.

993. As used in this article, "holder of the privilege" means:

- (a) The patient when he has no guardian or conservator.
- (b) A guardian or conservator of the patient when the patient has a guardian or conservator.
- (c) The personal representative of the patient if the patient is dead.

994. Subject to Section 912 and except as otherwise provided in this article, the patient, whether or not a party, has a privilege to refuse to disclose, and to prevent another from disclosing, a confidential communication between patient and physician if the privilege is claimed by:

- (a) The holder of the privilege;
- (b) A person who is authorized to claim the privilege by the holder of the privilege; or
- (c) The person who was the physician at the time of the confidential communication, but such person may not claim the privilege if there is no holder of the privilege in existence or if he is otherwise instructed by a person authorized to permit disclosure.

995. The physician who received or made a communication subject to the privilege under this article shall claim the privilege whenever he is present when the communication is sought to be disclosed and is authorized to claim the privilege under subdivision (c) of Section 994.

996. There is no privilege under this article as to a communication relevant to an issue concerning the condition of the patient if such issue has been tendered by:

- (a) The patient;
- (b) Any party claiming through or under the patient;
- (c) Any party claiming as a beneficiary of the patient through a contract to which the patient is or was a party; or
- (d) The plaintiff in an action brought under Section 376 or 377 of the Code of Civil Procedure for damages for the injury or death of the patient.

997. There is no privilege under this article if the services of the physician were sought or obtained to enable or aid anyone to commit or plan to commit a crime or a tort or to escape detection or apprehension after the commission of a crime or a tort.

998. There is no privilege under this article in a criminal proceeding.

1012. As used in this article, "confidential communication between patient and psychotherapist" means information, including information obtained by an examination of the patient, transmitted between a patient and his psychotherapist in the course of that relationship and in confidence by a means which, so far as the patient is aware, discloses the information to no third persons other than those who are present to further the interest of the patient in the consultation or examination or those to whom disclosure is reasonably necessary for the transmission of the information or the accomplishment of the purpose of the consultation or examination, and includes advice given by the psychotherapist in the course of that relationship.

1013. As used in this article, "holder of the privilege" means:

- (a) The patient when he has no guardian or conservator.
- (b) A guardian or conservator of the patient when the patient has a guardian or conservator.
- (c) The personal representative of the patient if the patient is dead.

1014. Subject to Section 912 and except as otherwise provided in this article, the patient, whether or not a party, has a privilege to refuse to disclose, and to prevent another from disclosing, a confidential communication between patient and psychotherapist if the privilege is claimed by:

- (a) The holder of the privilege;
- (b) A person who is authorized to claim the privilege by the holder of the privilege; or
- (c) The person who was the psychotherapist at the time of the confidential communication, but such person may not claim the privilege if there is no holder of the privilege in existence or if he is otherwise instructed by a person authorized to permit disclosure.

1015. The psychotherapist who received or made a communication subject to the privilege under this article shall claim the privilege whenever he is present when the communication is sought to be disclosed and is authorized to claim the privilege under subdivision (c) of Section 1014.

1016. There is no privilege under this article as to a communication relevant to an issue concerning the mental or emotional condition of the patient if such issue has been tendered by:

- (a) The patient;
- (b) Any party claiming through or under the patient;
- (c) Any party claiming as a beneficiary of the patient through a contract to which the patient is or was a party; or
- (d) The plaintiff in an action brought under Section 376 or 377 of the Code of Civil Procedure for damages for the injury or death of the patient.

1017. There is no privilege under this article if the psychotherapist is appointed by order of a court to examine the patient, but this exception does not apply where the psychotherapist is appointed by order of the court upon the request of the lawyer for the defendant in a criminal proceeding in order to provide the lawyer with information needed so that he may advise the defendant whether to enter a plea based on insanity or to present a defense based on his mental or emotional condition.

1018. There is no privilege under this article if the services of the psychotherapist were sought or obtained to enable or aid anyone to commit or plan to commit a crime or a tort or to escape detection or apprehension after the commission of a crime or a tort.



999. There is no privilege under this article in a proceeding to recover damages on account of conduct of the patient which constitutes a crime.

1000. There is no privilege under this article as to a communication relevant to an issue between parties all of whom claim through a deceased patient, regardless of whether the claims are by testate or intestate succession or by inter vivos transaction.

1001. There is no privilege under this article as to a communication relevant to an issue of breach, by the physician or by the patient, of a duty arising out of the physician-patient relationship.

1002. There is no privilege under this article as to a communication relevant to an issue concerning the intention of a patient, now deceased, with respect to a deed of conveyance, will, or other writing, executed by the patient, purporting to affect an interest in property.

1003. There is no privilege under this article as to a communication relevant to an issue concerning the validity of a deed of conveyance, will, or other writing, executed by a patient, now deceased, purporting to affect an interest in property.

1004. There is no privilege under this article in a proceeding to commit the patient or otherwise place him or his property, or both, under the control of another because of his alleged mental or physical condition.

1005. There is no privilege under this article in a proceeding brought by or on behalf of the patient to establish his competence.

1006. There is no privilege under this article as to information that the physician or the patient is required to report to a public employee, or as to information required to be recorded in a public office, if such report or record is open to public inspection.

1007. There is no privilege under this article in a proceeding brought by a public entity to determine whether a right, authority, license, or privilege (including the right or privilege to be employed by the public entity or to hold a public office) should be revoked, suspended, terminated, limited, or conditioned.

1019. There is no privilege under this article as to a communication relevant to an issue between parties all of whom claim through a deceased patient, regardless of whether the claims are by testate or intestate succession or by inter vivos transaction.

1020. There is no privilege under this article as to a communication relevant to an issue of breach, by the psychotherapist or by the patient, of a duty arising out of the psychotherapist-patient relationship.

1021. There is no privilege under this article as to a communication relevant to an issue concerning the intention of a patient, now deceased, with respect to a deed of conveyance, will, or other writing, executed by the patient, purporting to affect an interest in property.

1022. There is no privilege under this article as to a communication relevant to an issue concerning the validity of a deed of conveyance, will, or other writing, executed by a patient, now deceased, purporting to affect an interest in property.

1023. There is no privilege under this article in a proceeding under Chapter 6 (commencing with Section 1367) of Title 10 of Part 2 of the Penal Code initiated at the request of the defendant in a criminal action to determine his sanity.

1024. There is no privilege under this article if the psychotherapist has reasonable cause to believe that the patient is in such mental or emotional condition as to be dangerous to himself or to the person or property of another and that disclosure of the communication is necessary to prevent the threatened danger.

1025. There is no privilege under this article in a proceeding brought by or on behalf of the patient to establish his competence.

1026. There is no privilege under this article as to information that the psychotherapist or the patient is required to report to a public employee or as to information required to be recorded in a public office, if such report or record is open to public inspection.

# Congenital Anomalies And Congenital Adrenal Hyperplasia

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■ *Among 74 patients with congenital adrenal hyperplasia observed at Childrens Hospital, Los Angeles, in a 25-year period, 36 had the simple virilizing type and 38 the salt-losing type. During the same time, seven children with virilizing adrenal tumors were observed at the hospital.*

*While virilization and dehydration were the most common presenting symptoms, some of the children first came to medical attention because of other symptoms, and 11 of them died before adrenal hyperplasia had been diagnosed. Twenty-eight additional congenital cardiovascular, genitourinary, and gastrointestinal anomalies were found in 16 of these 74 children.*

*With proper management, the patients tolerated such stresses as surgical operation and infections without difficulty.*

CHILDREN WITH CONGENITAL adrenal hyperplasia present three important challenges to the physician. First, the problem of making the original diagnosis may be a life-saving accomplishment. Second, given a child with this illness, proper therapy can reduce the possibility of death during a childhood illness or surgical operation. Third, therapy can eliminate the problems of virilization during childhood and the premature fusion of bony epiphyses which finally results in short stature.

Because of the impression given in the medical literature that other congenital anomalies are rare in these children, this report summarizes the significant features from 74 children with congenital adrenal hyperplasia, 16 of whom had other congenital anomalies. Diagnostic and therapeutic recommendations which are based upon this experience and reports from other institutions<sup>7-10,12</sup> are also presented.

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Submitted 30 September 1965.

## Methods

The children with congenital adrenal hyperplasia who are reported upon herein have all been seen at the Childrens Hospital of Los Angeles and have been observed in the Endocrine Clinic for periods up to 18 years. Some of the data have been obtained from a review of all hospital charts up to 1965 which were coded under any of the following terms: congenital adrenal hyperplasia, adrenal cortical hyperfunction, adrenal tumor and adrenal adenoma and adenocarcinoma. Further data were obtained from records kept in the Endocrinology Division of additional patients who had not been admitted to the hospital but were seen in the Endocrine Clinic.

## Results

### *Sex Incidence and Mortality*

The data in Table 1 summarizes the sex incidence and mortality rate among 74 children with congenital adrenal hyperplasia who were observed at Childrens Hospital in the years 1941-1965.



TABLE 1.—*Congenital Adrenal Hyperplasia*

	Simple Virilizing Type			Salt Losing Type		
	Total	Living	Dead	Total	Living	Dead
Male .....	12	7	5	19	15	4
Female .....	24	16	8	19	11	8
	36	23	13	38	26	12

There were 36 children with the simple virilizing type of the disease and 38 with the salt-losing type. No cases of hypertensive type or 3- $\beta$  dehydrogenase deficiency type of adrenal hyperplasia, which were recently reviewed by Bongiovanni,<sup>5</sup> have been recognized at this hospital. A greater incidence of adrenal hyperplasia in females than males is evident in the simple virilizing type, and not in the salt-losing type.

Mortality was unusually high in the simple virilizing type. (This will be discussed later.) Of the 74 children with congenital adrenal hyperplasia, 49 are now\* living and 25 are dead.

Chart 1 shows the incidence and mortality of new cases of congenital adrenal hyperplasia at Childrens Hospital from 1941-1965. The great increase in cases from 1946-1955 probably reflects improvement in record-keeping and coding of diagnoses. The gradually decreasing number of cases since 1945 may indicate the growth of nearby hospitals where these children are now being seen. The definite drop in mortality after 1950, when therapy with cortisol was begun, is apparent.

#### Genetics

Table 2 summarizes data about the siblings of 69 of the 74 patients with congenital adrenal hyperplasia. Of a total of 101 siblings, 14 are known to have the disease, and five of these have been observed at Childrens Hospital. Affected siblings had the same type of adrenal hyperplasia as the patient. Nearly one-fourth of the siblings of children with the salt-losing type also had the disease, but of 46 siblings of children with the simple virilizing type, only two were known to be affected. None of the parents were known to have adrenal hyperplasia.

#### Presenting Symptoms and Diagnosis

The most diagnostic signs and symptoms in these children, summarized in Table 3, were enlargement of the penis or clitoris, vomiting and dehydration, pubic hair and excessive growth. Seven of the girls were originally thought to be boys with hypospadias and undescended testes.

The diagnosis was much more difficult, and usually not established during life, when the presenting problems were jaundice, cyanosis and dyspnea, omphalocele, erythroblastosis, meningitis or tracheoesophageal fistula. Two children were originally studied because a sibling had congenital adrenal hyperplasia.

Since virilization is the clinical finding most helpful in the diagnosis of adrenal hyperplasia, the cases of virilizing adrenal tumors were also reviewed. Among 11 children with histologically proven adrenal adenocarcinoma and one with adrenal adenoma seen at Childrens Hospital between 1941 and 1965, six of those with adenocarcinoma (five girls, one boy) and the one with adenoma (a boy) first came to medical attention because of virilization. Between the ages of one and four years they had begun to have enlargement of the penis or clitoris, pubic hair, acne and

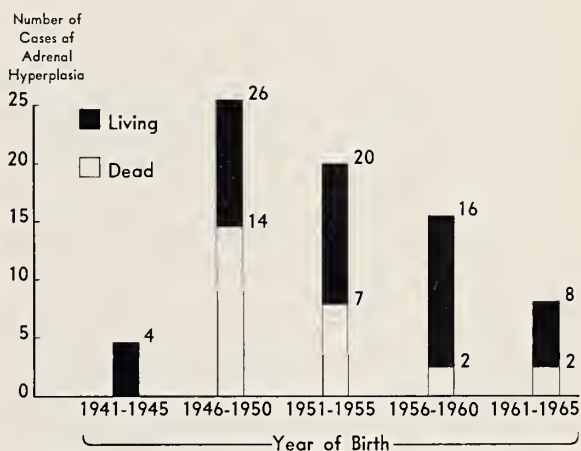


Chart 1.—Cases of congenital adrenal hyperplasia are divided into five-year intervals depending on the year of birth. Beginning with 1951-1955 when cortisone therapy was begun, the decrease in mortality is apparent.

TABLE 2.—*Related Data on 101 Siblings of 69 Patients*

	Type of Disease	
	Simple Virilizing	Salt-Losing
Affected .....	2	12
Non-affected .....	44	43
Total .....	46	55

\*September 1965.

	36 Males	Incidence	38 Females	Incidence
enlarged penis .....	11		enlarged clitoris .....	32
vomiting and dehydration.....	13		vomiting and dehydration .....	12
pubic hair .....	4		pubic hair .....	6
failure to thrive .....	7		undescended testes and hypospadias....	7
excessive growth .....	3		excessive growth .....	3
jaundice .....	2		cyanosis and dyspnea.....	5
omphalocele .....	1		erythroblastosis .....	3
convulsions .....	2		family history .....	2
acne .....	2		meningitis .....	1
			tracheoesophageal fistula .....	1

TABLE 4.—Results of Laboratory Studies Before Therapy

Type of Disease	Serum Na (mEq per L)	Number of Cases	Serum K (mEq per L)	Number of Cases	Urine 17-KS (mg per 24 Hours)	Number of Cases	Urine Pregnanetriol (mg per 24 Hours)	Number of Cases
Virilizing .....	134-155	18	4.3- 6.0	15	3.2-34.6	22	4.2-22.0	6
Salt-Losing .....	113-145	29	4.2-10.3	28	1.0-23.0	22	0.3- 6.6	11

accelerated growth. In these seven children with virilization, urinary 17-ketosteroids (mg per 24 hours) were: 4.8, 5.2, 10.4, 14.0, 15.9, 56.3 and 93.5; and the urinary pregnanetriol content (mg per 24 hours) in three of them was: 1.2, 1.2 and 1.7. Two of them had a small palpable abdominal mass; and in six of them intravenous pyelograms were interpreted to indicate adrenal tumors. The five girls, from whom the virilizing adrenal adenocarcinomas were removed surgically, were living and well at last report (from three to nine years after operation).

#### Laboratory Studies

Table 4 summarizes the pertinent laboratory studies at the time the children were first seen. While there was a tendency to low serum sodium and high potassium concentration in the salt-losing type, these abnormalities were not always found, and in the virilizing type the sodium and potassium were always normal. The urinary 17-ketosteroids were invariably elevated in both types of adrenal hyperplasia, and urinary pregnanetriol was elevated (greater than 1.0 mg per 24 hours) in all but two children in whom it was measured. In the two exceptions the pregnanetriol content was 0.3 and 0.6 mg in 24 hours.

#### Associated Anomalies

There was a surprising variety and a high incidence of other severe congenital anomalies in the present series: 16 of the 74 children with congenital adrenal hyperplasia had at least one other inherent abnormality (Table 5). Cardiovascular anomalies included: transposition of the great vessels, arteriovenous communis, patent ductus arteriosus, endocardial fibrosis, ventricular and atrial septal defects and pulmonic stenosis. Eight

TABLE 5.—Congenital Anomalies in 74 Children with Congenital Adrenal Hyperplasia

Cardiovascular .....	8
Genitourinary:	
hydronephrosis .....	3
horseshoe kidney .....	1
urethrovesical fistula .....	1
urethrectal fistula .....	1
renal cortical cysts.....	1
undescended testes .....	1
Diaphragmatic hernia .....	2
Omphalocele .....	1
Accessory spleen .....	1
Bile duct hyperplasia .....	1
Cirrhosis .....	1
Torticollis .....	1
Stenosis of ileum.....	1
Inguinal hernia .....	1
Tracheoesophageal fistula .....	1
Mental retardation .....	2

TABLE 6.—Surgical Procedures Performed on 74 Children with Adrenal Hyperplasia

		Compli- cations
Adrenalectomy .....	6	none
Clitoridectomy and vaginoplasty.....	13	none
Laparotomy .....	9	none
Tonsillectomy .....	2	none
Appendectomy .....	1	none
Bladder neck resection.....	1	collapse
Mastoidectomy .....	1	none
Hepatic lobectomy and omphalocele repair..	1	died

children had significant genitourinary anomalies in addition to the common finding of genital enlargement and labial fusion. Prostatic enlargement resulting from excess androgens was thought to contribute to the hydronephrosis in two boys. Eleven other congenital anomalies found in these children are also summarized in the table.

#### Surgical Procedures

Table 6 summarizes the 31 surgical procedures which were done on these children. There has



been only one complication—sudden hypotension immediately following operation for bladder neck obstruction in a boy with a slightly enlarged penis at age 21 months. He was successfully treated with vasopressors and blood transfusions, and cortisol therapy was not begun until age 23 months when a diagnosis of congenital adrenal hyperplasia was established. The infant with omphalocele, congenital heart disease, diaphragmatic hernia and undescended testes died at age one day, after operation, and adrenal hyperplasia was a post-mortem diagnosis.

*Causes of Death*

Table 7 summarizes data on the age and the major problems in the 25 children with adrenal hyperplasia who died. Nine children died at ages under 11 months with dehydration probably related to the disease, and pneumonia and atelectasis was noted at autopsy in six of these. Meningitis and subdural hemorrhage were found in three children who died at 5, 9, and 17 days of age. Five children died at ages between one and eight months, with heart disease the main cause. Erythroblastosis at age one day, tracheoesophageal fistula at age three days, cirrhosis at age two months, and sepsis at ages five days, two months, and 22 months caused six other deaths.

In only three of these 25 children—the 22-month-old child with sepsis, the 28-month-old with convulsions and the four-year-old with encephalitis—had adrenal hyperplasia been diagnosed before the terminal illness. The first child became ill, did not receive parenteral therapy, and died 36 hours after onset of illness. The 28-month-old arrived at the hospital after sudden onset of convulsions, and died within hours despite therapy with desoxycorticosterone (DOCA) and hydrocortisone. Serum sodium and potassium concentrations were normal. The four-year-old girl with encephalitis had a brief illness consisting of fever, vomiting and convulsions, and then apnea within 24 hours. She had normal serum electrolytes on admission to the hospital, was maintained seven days with a respirator and finally died despite therapy with parenteral DOCA and cortisone.

**Therapeutic Recommendations**

*Cortisone Doses*

Table 8 summarizes the maintenance cortisone dose which the 49 living children are receiving. As with most medications—especially with cortisone

for this illness—the correct dose must be determined for each child. We see these children at intervals of three to six months and recommend x-ray studies to appraise bone development and also determinations of urinary 17-ketosteroids and pregnanetriol each six months. These studies are especially needed during puberty, for at that time we have seen the “bone age” advance as much as two years in a six-month interval because of inadequate cortisone therapy.

The cortisol dose is adjusted to keep the pregnanetriol excretion below 1 mg per 24 hours and the excretion of 17-ketosteroids at levels which are normal for the child’s age (below 1 mg up to age one year; 1 to 2 mg up to age five years; and below 4 mg up to age 10 years). With this follow-up program, it has been possible to maintain a normal rate of growth and normal increases in “bone age.”

*Salt-losing Type*

In addition to cortisol, the patients who have a demonstrated tendency to dehydration, hyperkalemia and hyponatremia have been treated initially with DOCA, 1 to 2 mg daily, by intramuscular injection. After their presenting problems have been stabilized they have usually been started on 9  $\alpha$ -fluorohydrocortisone (Florinef®) tablets, 0.05 to 0.1 mg daily. A few infants have been successfully treated with 20 to 25 mg intramuscular injections of Percorten trimethylacetate® at monthly intervals. From 1 to 3 grams of sodium chloride

TABLE 7.—*Causes of Death in 25 Children with Adrenal Hyperplasia*

	Number	Time After Birth
Dehydration, salt-depletion, hyperkalemia .....	9	1 to 11 months
Meningitis and cerebral hemorrhage .....	3	5 to 17 days
Congenital heart disease .....	5	1 to 8 months
Erythroblastosis .....	1	1 day
Cirrhosis .....	1	2 months
Sepsis .....	3	5 days, 2 months, 22 months
Hydronephrosis, convulsions, cerebral edema .....	1	28 months
Tracheoesophageal fistula .....	1	3 days
Encephalitis .....	1	4 years

TABLE 8.—*Therapeutic Doses of Cortisone at Various Ages for Patients with Congenital Adrenal Hyperplasia*

Age (Years)	Dose (mg per Day)
0 - 2	10 - 25
3 - 8	15 - 50
9 - 20	25 - 60

have usually been added to the diet of children under age one year. The dose of DOCA and 9  $\alpha$ -fluorohydrocortisone has been adjusted for each patient to an amount which maintains a normal serum sodium and potassium concentration and yet does not cause hypertension. We have found it necessary to measure blood pressure frequently during the first few weeks until a proper dose was discovered. Doses of the salt-retaining hormone have been tapered off at ages two to five years. Children with the salt-losing type should probably be kept on salt-retaining hormones until age four years, and when therapy is discontinued the child should be observed closely for changes in serum sodium and potassium concentration.

#### *Surgical Operations, Infections and Stress*

During surgical procedures or infections like measles or chickenpox, the dose of cortisone should be doubled, and we have commonly used parenteral hydrocortisone when there was vomiting and diarrhea. All patients with congenital adrenal hyperplasia, and especially if they are known to have the salt-losing type, should also receive salt-retaining hormones during surgical procedures. Since it is possible that an occasional patient with the simple virilizing type will turn out to be a salt-loser during stress, all children with adrenal hyperplasia require very careful observation when they have either infectious diseases or operations.

Surgical repair of the external genitalia in the girls, clitoridectomy and vaginoplasty, has usually been done between the ages two and four years. No complications have been associated with these procedures.

#### **Discussion**

Congenital adrenal hyperplasia of the simple virilizing type is thought to result from a congenital deficiency of adrenocortical 21-hydroxylase activity. The salt-losing type results from a more complete absence of this enzyme. The hypertensive type of adrenal hyperplasia results from a deficiency of 11-hydroxylase activity and the resulting excess production of the salt-retaining hormone, 11-desoxycorticosterone.<sup>3</sup> Deficiency of 3- $\beta$  hydroxysteroid dehydrogenase has also been reported to cause congenital adrenal hyperplasia<sup>4</sup>—but rarely.

In light of the absence of disease in parents and the high incidence of the disease noted in statistical studies of siblings these are thought to be recessively

inherited diseases. Childs and coworkers<sup>6</sup> reported data indicating that parents of these patients excrete significantly more pregnanetriol after ACTH stimulation than do normal controls, which is evidence supporting the concept that the parents are heterozygotes.

The sex ratio in the present series, 43 females to 31 males, was similar to that reported by other investigators. The relatively greater incidence of the simple virilizing type in females compared with the more equal sex incidence in the salt-losing type, was also found among the patients reported by Wilkins.<sup>12</sup> In the present series, approximately one-fourth of the siblings of patients with the salt-losing type also had the disease, but only two of 46 siblings of patients with the simple virilizing type had the disease.

These two findings, the slightly different sex incidence and the decidedly different incidence among siblings, might suggest that the inheritance of the two types is different. Two important factors which may have contributed to these two findings are: (1) the simple virilizing form of adrenal hyperplasia may manifest itself later in life and, therefore, the disease may still develop in some of these unaffected siblings; (2) in girls with the simple virilizing type the disease is more likely to be diagnosed because of an enlarged clitoris than are boys with an enlarged penis; hence the diagnosis of the simple virilizing type is more easily missed in boys.

While a high serum potassium and low serum sodium were common in the infants who died with this illness, they were not always found. While urinary 17-ketosteroids and pregnanetriol determinations will lead to the diagnosis in most of these patients, those rare children with the earlier metabolic blocks in adrenal steroid synthesis may have normal values.<sup>6</sup> Both vigilance and knowledge are required for diagnosis of this condition in young infants. The high mortality among this group of children, partly related to the surprising incidence of major associated anomalies, has made us very suspicious of this diagnosis in many sick children who did not have it. We have recommended consistently that sick infants suspected to have adrenal hyperplasia, should receive DOCA, 1 to 2 mg, intramuscularly, when the question first arises. This may be life-saving and will not obscure the diagnosis since it does not alter significantly the urinary steroid excretion.

Cleveland and coworkers<sup>7</sup> reviewed eight deaths



## A CHECK-LIST TO SAVE THE SALT-LOSER

- A. Think of salt-losing adrenal hyperplasia when:
  1. infants vomit, fail to gain weight, become dehydrated, or have any evidence of virilization (enlarged clitoris or penis, or labial fusion).
  2. infants have low serum sodium or high serum potassium.
- B. Give the infant desoxycorticosterone (DOCA), 2 mg intramuscularly each day, replace salt and water deficit, and determine blood pressure frequently.
- C. Confirm diagnosis by 24-hour urine collection analyzed for 17-ketosteroids and pregnanetriol.

among 92 patients receiving treatment for congenital adrenal hyperplasia. Two of these deaths may have resulted from giving too much saline solution to children receiving salt-retaining hormones. One had recurrent cerebral emboli from a cardiac mural thrombus, and one did not receive parenteral therapy during an acute illness. In four of the eight deaths studied by Cleveland, the manifestations of disease resembled those in the four-year-old and the 22-month-old patients reported herein. The patients had acute onset of fever, then they became comatose and collapsed and died after a brief illness dominated by symptoms referable to the central nervous system. None of the six children with these manifestations—the two in our series and the four whose deaths were studied by Cleveland—were believed to have died because of abnormalities in serum electrolytes; apparently they died of an acute encephalitis-like illness. While pseudotumor cerebri, which can be associated with adrenal steroid therapy, and especially during withdrawal of steroid therapy, was mentioned by Cleveland and coworkers as a possible factor, an as yet unknown relationship between adrenal hyperplasia and the central nervous system seems more likely.

The methods for distinguishing virilizing adrenal adenoma and carcinoma were discussed by Scarpa-Smith and coworkers<sup>11</sup> in their report of two children with virilizing adrenal tumors. The finding of elevated pregnanetriol, of suppression of 17-ketosteroid excretion by cortisone therapy, and of pronounced stimulation of 17-ketosteroid and pregnanetriol excretion by ACTH, all suggest a diagnosis of adrenal hyperplasia. The finding of elevated urinary dehydroepiandrosterone<sup>1</sup> would favor the diagnosis of adrenal tumor.

Other congenital defects have rarely been reported to be associated with congenital adrenal hyperplasia. A boy with third-degree hypospadias and salt-losing adrenal hyperplasia was reported by Blodgett and coworkers.<sup>2</sup> Testicular biopsy confirmed the sex in that case. In the present series seven girls were at first considered to be boys with third-degree hypospadias and undescended testes. Laparotomy and examination of buccal smear for sex chromatin were utilized to make the correct determination of sex in four of these cases and in three it was determined at autopsy. Twenty-eight congenital anomalies were present in 16 different children among the 74 cases reported here. Eleven of these children with additional anomalies died and adrenal hyperplasia was diagnosed at autopsy. This association between adrenal hyperplasia and other congenital anomalies has not previously been emphasized, and yet nearly half of the mortality rate in these 74 cases was accounted for by patients with these multiple anomalies. Diagnosis of adrenal hyperplasia, with or without associated anomalies, rests finally upon a physician with a high index of suspicion.

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# Hemorrhage During Long-Term Anticoagulant Drug Therapy

## Part IV. Selection and Management of Patients

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■ *Most serious hemorrhages that occur during long-term anticoagulant drug therapy are due either to poor patient selection or to poor management of the patient, or both.*

*In each patient being considered for treatment, the risk of bleeding must be evaluated and classified as high, moderate or low.*

*The clinician must especially assess the risk of intracranial hemorrhage in hypertensive patients, and must screen all patients for potential sources of gastrointestinal bleeding. There is ample time for such investigations, since initiating long-term anticoagulant therapy is not an emergency procedure.*

*The desired level of prothrombin activity must be adjusted to the risks determined for each individual patient. There is no single "therapeutic range" applicable to all patients with their varying hemorrhagenic risks.*

*Proper management includes sufficient laboratory testing to maintain the desired prothrombin level, and continued vigilance to detect signs of early bleeding.*

*Preventable hemorrhage cannot be cited as evidence against the value of anticoagulant drug therapy.*

PREVIOUS STUDIES in this series have established that the chief risk in long-term anticoagulant drug therapy is that of intracranial and gastrointestinal hemorrhages, which constitute 90 per cent of the serious hemorrhages complicating this therapy. The chief factor in these hemorrhages is not the hypocoagulable state but the underlying lesion. Minor bleeding, although it sometimes precedes a serious hemorrhage, is not to be regarded as premonitory.<sup>2-4</sup>

Those serious hemorrhages which could be avoided by early detection of potential causative lesions and by better management should not be

cited as evidence against anticoagulant therapy. As Miale<sup>15a</sup> wryly observed, after bleeding there is "... an almost uncontrollable urge to blame someone or something; the laboratory, the thromboplastin used or, periodically, the test used in regulating therapy ...". The tendency has been to investigate thoroughly only *after* bleeding or unexplained anemia occurs, and thus the emphasis has been placed on the complications rather than on the practical aim: to avoid the avoidable hemorrhages.

The first step before beginning long-term anticoagulant therapy is a physical examination, at least as thorough as the annual examination of a healthy person, to identify bleeding or potentially hemorrhagenic lesions.<sup>1</sup> Only then is it possible to

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balance intelligently the risk of bleeding against the danger of thromboembolism. Where the danger is great, even the high risk presented by a potentially hemorrhagic lesion may be justified; or a more moderate hypocoagulability may avoid extreme risk from hemorrhage with reasonable protection against thrombosis.

About 10 per cent of all serious hemorrhages associated with anticoagulant therapy occur at sites where they are rarely predictable (the adrenal glands, pancreas, spinal cord, in intramural intestinal and retroperitoneal spaces and in the ovaries). This study is concerned only with the intracranial and gastrointestinal hemorrhages, which constitute the preponderant risk. It attempts to answer the following questions:

1. What is the quantitative risk of these serious hemorrhages?
2. What criteria govern anticoagulant therapy in hypertensive patients?
3. What factors govern the risk of serious gastrointestinal hemorrhages?
  - (a) How is the actively bleeding lesion to be detected?
  - (b) How is the potentially hemorrhagenic lesion to be detected?
  - (c) How is the risk in these conditions to be determined?
4. What are clinically "safe" and "unsafe" levels of prothrombin activity?

#### *What Is the Quantitative Risk of Serious Hemorrhage?*

Previous studies have restricted the preponderance of risk to hypertensive patients and those with gastrointestinal lesions—and, more specifically, (1) to those hypertensive patients who have an intracranial hemorrhage as a natural complication and, (2) to gastrointestinal lesions that are actively bleeding. Other causes of hemorrhage—a bleeding diathesis, renal or liver disease, avitaminosis, vasculitis—are usually detectable through a careful history, physical examination and indicated laboratory studies.<sup>1</sup>

The overall risk of nontraumatic hemorrhage in long-term anticoagulant therapy has been estimated at one in every 10 treatment years.<sup>10</sup> The risk of serious hemorrhage is much lower: In 622 cases treated for an average of 1.6 years there were 23 serious hemorrhages, or one in every 43 years.<sup>2,3</sup> Even in test periods in which the prothrombin content was found to be below the pre-

sumably "safe" minimum, the incidence of serious hemorrhage was low: nine in 1,985 "unsafe" periods, or 0.4 per cent.<sup>2,3</sup> Borchgrevink cited a comparable incidence of 0.3 per cent.<sup>8</sup>

#### *What Criteria Govern Anticoagulant Therapy in Hypersensitive Patients?*

There is little evidence that the anticoagulant drugs in less than toxic doses *initiate* serious bleeding, but within the therapeutic range of hypocoagulability minor bleeding may be *converted* into serious hemorrhage. In hypertensive patients the chief risk is intensifying a naturally occurring cerebral hemorrhage. The risk of cerebral hemorrhage occurring in the course of the natural history of hypertension can be estimated only statistically.

Evaluation of the degree of damage of cerebral blood vessels in an individual is difficult. Cerebral arteriography before treatment is seldom employed or indicated. A deep intracerebral hemorrhage may occur without blood appearing in the spinal fluid and may mimic a cerebral thrombosis or tumor.

In prolonged hypertension, damage to the cerebral arteries and underlying tissues leads to intracranial hemorrhage as a natural consequence in 10 to 30 per cent of patients. Anticoagulant therapy may be too great a risk except for patients in the greatest danger of thrombosis. In rapidly progressing thrombosis in the vertebral basilar system, Millikan<sup>17</sup> would accept the risk of anticoagulant therapy even with blood pressure at 240/140 mm of mercury but would attempt by antihypertensive drugs to reduce pressure to 180/110 mm. Wright<sup>27</sup> agreed that pressure above 180/110 mm definitely increases the risk of intracranial hemorrhage but said that in a patient who has had recurrent thrombosis "a calculated risk may be acceptable in order to treat this threatening problem." He gave anticoagulant therapy to patients with average blood pressures of 230/120 mm who had had from three to seven thrombotic episodes before anticoagulant therapy, and continued it for five years or more without subsequent hemorrhage or thrombosis. Ideally, he preferred to maintain diastolic blood pressure below 100 mm of mercury.

#### *What Factors Govern the Risk of Serious Gastrointestinal Hemorrhage?*

No hemorrhage is "spontaneous" in the sense that bleeding is caused by hypocoagulability alone, without vascular damage. Probably 20 per cent

of patients for whom long-term anticoagulant therapy is considered either have or will have potentially hemorrhagic gastrointestinal lesions.<sup>8</sup> How many of these can be detected before therapy is begun?

As reported previously in this series,<sup>3</sup> in 77 cases of gastrointestinal hemorrhage occurring in long-term therapy, the causative lesions had been identified previously in only seven instances (in which the risk of therapy was presumably considered justified). In 37 others, lesions were found after hemorrhage. Thirty of the 37 presumably could have been detected before: 15 ulcers, eight neoplasms, four cases of diverticulitis, three hiatal hernias. The other lesions probably could not have been detected before the bleeding episode; cirrhosis of the liver with esophageal varices in two cases, acute gastritis in three, "inflammation" in two. The danger of diverticulosis as a cause of massive colonic bleeding was recently emphasized by Smith and Berne<sup>24</sup>: "... the patient must be asked particularly about . . . any chronic use of drugs, especially anticoagulant therapy . . ."

*Detection of Lesions.* Peptic ulcer is believed to be present in 10 per cent or more of male adults and is significantly more frequent in those with coronary sclerosis. Of 203 patients treated by Borchgrevink<sup>8</sup> for coronary sclerosis, 39 (19 per cent) had had previous diagnosis of peptic ulcer by roentgen study. Sevitt<sup>23</sup> warned that "the possibility of silent peptic ulceration, which may bleed perhaps copiously or even fatally during therapy, has to be continuously borne in mind."

Neoplasms, diverticulitis and hiatal hernias can be suspected only from history and findings on examination. Gastric erosion by salicylates, steroid drugs, phenylbutazone or alcohol most often cannot be proved but must be presumed from the history of previous ingestion. The same is true of bleeding from capillaries damaged by anticoagulant drugs. Acute hemorrhagic lesions often are not detected by roentgenographic studies after hemorrhage,<sup>29</sup> but most chronic lesions, if suspected, can be identified.

Investigative measures considered routine in periodic examinations of healthy persons (proctoscopy, for example, and fecal tests) often are not done as a preliminary to long-term anticoagulant therapy although they are far more important in determining potential bleeding sites *before* hemorrhage than after. Yet many reports on hemorrhage do not mention that fecal specimens tested

before therapy were free of blood or that in patients with healed ulcers fecal tests were repeated periodically. The necessity of withholding red meat from the diet for three to four days to eliminate falsely positive results has undoubtedly limited use of the test for routine "screening" for significant gastrointestinal bleeding.<sup>13</sup>

Bjerkelund<sup>7</sup> did not exclude patients with gastrointestinal lesions and made no periodic fecal examinations; of his seven patients with gastrointestinal hemorrhage, six had lesions that had been previously detected. "Active peptic ulceration" was considered reason for withholding anticoagulant therapy in the study of the Medical Research Council of the British Medical Association,<sup>15</sup> but the diagnosis was based only on clinical findings, and hemorrhage occurred in two patients with peptic ulcer among 195 treated. That a "careful" clinical history may not be careful enough for disclosure of ulcer symptoms is indicated by Fisher<sup>11</sup>: "Intense inquiry" *after* upper gastrointestinal hemorrhage occurring during anticoagulant therapy elicited a history indicative of gastrointestinal ulceration in most of his patients. Seaman<sup>21</sup> likewise concluded that the diligence with which the patient is questioned determines the likelihood of anticipating potential causes of hemorrhage.

In a double-blind controlled clinical test<sup>22</sup> in which negative results were required in three gum guaiac fecal tests before anticoagulant therapy was begun, gastrointestinal bleeding occurred as frequently in the treated as in untreated groups. This suggests that bleeding lesions developed after treatment was begun and emphasizes the need for periodic testing.

*How Is Risk to Be Determined?* Before long-term anticoagulant drug therapy can be considered properly selected for the patient, these minimal precautions should be taken except in unusual circumstances:

1. Meticulous inquiry regarding present or past manifestations of a gastrointestinal lesion.
2. Routine sigmoidoscopy.
3. Routine fecal study for the presence of blood.
4. Appropriate roentgen study of any manifestations of bleeding lesions.
5. On diagnosis of peptic ulcer, evaluation of its condition—that is, healed, active without bleeding, or actively bleeding.

*Management.* Several principles in management logically should be applied. First, the highest de-



gree of care should be given to those patients with the greatest risk of serious hemorrhage—the hypertensive patients and those with gastrointestinal lesions. The risk of fatal or crippling thromboembolism without anticoagulant therapy must be carefully evaluated. For these patients, the compensating factor is greater care: as Sevitt says,<sup>23</sup> less drug, more care and probably more prothrombin tests. In addition, those with healed gastrointestinal lesions must have more frequent fecal tests for blood. Since these lesions, if reactivated, may bleed even with the blood in the normal state of coagulability, they may the more likely bleed at a “safe” prothrombin level.<sup>3</sup>

#### *What Are Clinically “Safe” and “Unsafe” Levels of Prothrombin Activity?*

Discussion of “safe” and “unsafe” prothrombin levels has unfortunately often led to implicit reliance on those indices and subsequently to reports by puzzled physicians of hemorrhage occurring “even though the prothrombin activity was in the therapeutic range.” But the critical level must always be a matter of individual estimate, determined from all that can be learned about the integrity of the patient’s blood vessels.

Bleeding was first correlated with prothrombin deficiency because this was the coagulation factor first observed to be affected by coumarin. “Safe” levels of prothrombin were then determined, above which hemorrhage was thought to be unlikely. When bleeding without discernible cause occurred at these safe levels (as measured by the original one-stage Quick test) it was thought to be caused by deficiency in other coagulation factors also depressed by coumarin (factor VII, proconvertin; factor IX, plasma thromboplastin component; factor X, Stuart-Prower factor).

The primary importance of the vascular break as the cause of bleeding was early shown in studies on man and animals. Dogs, rats and rabbits with prothrombin time from four to 10 minutes had no tendency to hemorrhage.<sup>14</sup> Many critical studies were reported in which the prothrombin time was excessively long yet no bleeding occurred. Brambel<sup>9</sup> in 1949 discussed some patients in whom Dicumarol had rendered the blood completely incoagulable. Wright<sup>28</sup> described a patient with extreme hypoproteinemia with no prothrombin content shown by the two-stage technique, who had no bleeding although the prothrombin time was eight minutes.

“When the vascular system is intact,” Quick said,<sup>20</sup> “an individual will not hemorrhage even though his blood is incoagulable. . . . Hemorrhage occurs only when an additional factor is superimposed on the original coagulation defect.” Hjort and Hasselback<sup>12</sup> agreed: “. . . breakdown of the clotting mechanism does not in itself produce bleeding: spontaneous bleeding occurs only when the vascular stress or injury is superimposed on a failing coagulation system.” Stern and Dreskin<sup>25</sup> and also Mickerson<sup>16</sup> likewise emphasized that vascular damage is necessary for bleeding to occur. The site of damage (capillary, venous or arterial) localizes the site of potential bleeding, and the character of the vascular break determines the degree of hypocoagulability at which bleeding becomes serious.

No blood test can measure the presence or the character of a break in an internal blood vessel. The estimate of the risk of serious bleeding, then, is actually an evaluation of the integrity of the blood vessels. Borchgrevink<sup>8</sup> has said that the antithrombotic “prophylactic effect . . . probably increases progressively to a P-P [prothrombin-pre-convertin] level of zero per cent.” Concomitantly, the risk of bleeding, if already present, also progressively increases with the reduction of prothrombin activity. Owren<sup>18</sup> expressed belief that this risk becomes critical only when coagulability is below 10 per cent by the P-P test.<sup>18</sup> Borchgrevink<sup>8</sup> also believes the risk of bleeding “may be ignored above a P-P level of 10 per cent” (equivalent to 20 per cent by the Quick one-stage test).

But no such average figure can apply accurately to two groups which differ critically in another respect: the presence or absence of a hemorrhagic lesion. For those so endangered, the desirable level is in the upper therapeutic range—low enough to make thrombosis unlikely, high enough to keep hemorrhage controllable. Bjerkelund<sup>7</sup> considered the “therapeutic optimal” range to be 10 to 30 per cent (P-P), although for “clinical hypertension” he preferred 20 to 40 per cent. Tulloch and Wright,<sup>26</sup> using the Quick one-stage test with a normal measure of 14 to 16 seconds, accepted 30 seconds as the therapeutic optimum but moderated this to 25 seconds “for a variety of specific reasons” which undoubtedly included an increased danger of hemorrhage. There is little evidence in clinical reports, though, that hypertensive patients are tested more frequently for better maintenance of the optimal level. In many hypertensive patients

the prothrombin content at the time of bleeding has been excessively low. Baker<sup>5</sup> attributed many intracranial hemorrhages to inadequate management.

### *What Is the Desirable Level in Those With Gastrointestinal Lesions?*

The risk of gastrointestinal bleeding and the adjustment of "the therapeutic range" depends on whether a gastrointestinal lesion is healed, is active without bleeding or is active with bleeding. Most clinicians agree that a healed lesion represents no increased risk; some believe that an "active lesion without bleeding" is no increased risk, and some even suggest that active lesions with bleeding may be treated without an increased risk if the bleeding is not severe.<sup>19</sup>

Bay and his associates<sup>6</sup> on two occasions treated acute coronary thrombosis in a patient who twice had bled from a peptic ulcer. No bleeding occurred in either of these treatments, or in a year of continuing therapy following the second occlusion; after that a massive gastric hemorrhage occurred, when the prothrombin time was just over twice the control. The patient recovered and at his insistence the anticoagulant therapy was continued. Borchgrevink<sup>8</sup> detected duodenal ulcer radiographically in two patients with no sign of bleeding; he continued therapy "while the ulcers healed."

Owren<sup>19</sup> said he continues treatment even if bleeding from a stomach ulcer or other lesions occurs, as long as it is not severe, believing that at a "thrombotest" value of 20 per cent the hemostatic mechanism is normal. Most clinicians do not agree, however, and feel strongly that the patient with a bleeding peptic ulcer should not receive long-term anticoagulant therapy unless the threat of impending thromboembolism is very great.

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# Outlook for Restrictive Animal Legislation in the 89th Congress

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■ *Past records indicate that legislation, be it extreme or moderate in design, will be the goal of the proponents of restrictive animal legislation in the 89th Congress. Bills similar to those introduced in past sessions almost surely will appear again. If the President succeeds in soliciting congressional support for his goals of the Great Society, Congress may have little time for other legislative matters. The medical and scientific forces that oppose the use of federal legislation as a means of upgrading the standards of animal care and improving the validity of the results of biological research can be expected to continue their support of voluntary control through education and research. Continued support of the effective "task forces" and public relations programs that developed during the 88th Congress must come from all segments of the organized health professions.*

SINCE EARLY IN THE 20th century, antivivisectionists in the United States have attempted to do what their British counterparts accomplished in 1876, namely, to obtain enactment of national legislation restricting animal experimentation on the grounds of humane concern for animals. The fact that every single one of the 50 states has an anticruelty statute and that, in addition, some states have special laboratory control systems has not diminished the ardor and cunning of the proponents of legislation to curtail the scientific use of animals. If the people of this country are to benefit from the unrestricted development of new medical knowledge, new drugs and new technical procedures, every physician must maintain a continuing vigilant attitude toward the threat of legislative action.

During the 88th Congress 11 bills, each of which would provide some degree of regulation

in the use of animals in medical research and teaching, were placed in the legislative hopper. Fortunately, Congress gave no formal consideration to any of the bills. Nine bills concerned with laboratory animal care and use were introduced into the first session of the Congress. The provisions of these bills are now familiar to most biological scientists. Five of the bills—S. 533 (Clark-Neuberger-Young), H.R. 4620 (Ashley), H.R. 4856 (Randall), H.R. 8077 (Pepper), and H.R. 5430 (Ashley) were exclusively restrictive and punitive. Provisions included individual licensing requirements, restrictions on experimental procedures, submission of project plans, and authority by the administrator to limit arbitrarily the number of animals used in an experiment. H.R. 4856 (Randall) and its identical companion, H.R. 8077 (Pepper), in addition, provided that a commissioner (specifically, a non-scientist) hold public hearings on any and all allegations presented by any humane society. Enforcement would be assigned to the Justice Department.

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The remaining bills were introduced later in the Congressional session. S. 1041 (Randolph), H.R. 4840 (Fogarty), and H.R. 4843 (Roberts) provided for the establishment of animal care standards and encouraged research and training, thereby being more constructive than other bills. Unfortunately, these still were primarily regulatory proposals. In October 1963, H.R. 8957 was introduced by Congressman Roybal of California. It provided for constructive programs for the advancement of laboratory animal care and for the establishment of standards. The Roybal bill was expected to become a rallying point for members of Congress who felt that they must state what they did favor in the way of legislation when they told their constituents that they did not approve the restrictive bills.

On 17 August 1964, Representative Paul Rogers of Florida introduced H.R. 12408 on behalf of the American Humane Association. The latter is the respectable national organization of the humane movement representing about 600 local and state humane associations. The Rogers bill copied the Roberts and Fogarty bills in its title and in providing for: (a) promulgation of standards for the humane care, handling and treatment of laboratory animals, and (b) authorization of helpful progress for the advancement of laboratory animal care by the Department of Health, Education, and Welfare. This bill specifically called for inspection of animal laboratories. It also provided for public hearings regarding changes in animal care standards. It followed the Roybal bill in calling for an advisory committee to recommend standards, propose rules and regulations and to promote cooperation by interested parties. The Rogers bill specified that three members of the committee of 13 should be chosen from the organized humane movement.

An analysis of the 11 bills shows clearly the positions that were occupied by the various forces drawn up for legislative battle. First, the position of the classical antivivisectionist was defended by bills S. 533, H.R. 4620, H.R. 5430, H.R. 4856 and H.R. 8077. The intent of those who support this position is not immediately clear unless one studies the development of the antivivisectionist movement. On the basis of the record of those who have opposed the use of animals in biological experimentation since the time of Claude Bernard in the 19th century, it must be concluded that the objective is the abolition, or at least minimization,

of the use of animals in research and teaching. Many well-intentioned and responsible persons have been drawn into this position, not realizing what eventual objectives are being pursued by their leaders who crusade in the name of the humane treatment of animals, a position that *all* people can support. Four organizations are providing essentially antivivisectionist leadership of this kind. They are the Humane Society of the United States, the Society for Animal Protective Legislation, the Animal Welfare Institute and the National Catholic Society for Animal Welfare (no official connection with the Catholic Church).

The *second* position was that supported by the American Humane Association, the American Society for the Prevention of Cruelty to Animals and other groups. Such bills as H.R. 12408, H.R. 4843 and H.R. 4840 did not provide exclusively for punitive and restrictive controls, but attempted to define a constructive approach through the establishment of standards for laboratory animal care, promotion of research, etc. Some biological scientists supported this position. The objection to support of this position is not always the content of the proposed bills nor the underlying philosophy. It is the inherent danger in any censorship of creative scientific endeavor. The legislation itself may be benevolent in its intent, but once enacted it would require continual vigilance, since it serves as a new instrument by which the antivivisectionists might harass biological scientists. Furthermore, if Congress is persuaded that some restrictions on animal utilization are needed, it might later be persuaded that additional restrictions are necessary. This position should not be supported because it is, basically, a negative position.

The *third* position is held by those who oppose any federal *regulatory* legislation. This is the position supported by the large segment of the scientific community. It is a position that many lay people have difficulty in understanding because of the inaccurate and misleading propaganda to which they have been exposed, namely, that medical researchers are irresponsible in the care of experimental animals. Medical scientists, on the contrary, are responsible people and are opposed to the inhumane treatment of animals. Jack O. Knowles, D.V.M., past president of the American Veterinary Medical Association, has stated: "For a profession to permit any agency, private or governmental, to police its activities strikes against the very heart of professional integrity and self-



reliance. It is not merely the falsehood of the basic premise of the bills—that animals are routinely ill-treated in laboratories—that arouses our opposition; abuses of laboratory animals are the rare exception, not the rule. Our fight is to prevent the use of an intrinsically good cause, humaneness, as a means to rally public sentiment in support of a movement that believes that only the Federal Government has the ultimate answer to all of our problems.”

F. J. L. Blasingame, M.D., executive vice-president of the American Medical Association, said: “This legislation implies a shocking and unjustified indictment of scientists and doctors which is unwarranted. The implication of the proposals is that far from being concerned with bringing possible relief and benefit to mankind, and indeed to animals, such physicians and scientists are mean, cruel and sadistic, requiring police action to control them. Existing state and municipal laws, university rules and regulations, codes of ethics, and the actual requirements of scientific research are adequate to secure and protect the objectives of the proposed legislation.”

Through the combined efforts of medical scientists, clinicians, educators, students, and a host of professional and concerned organizations, the climate in opposition to restrictive animal legislation has been improved materially. Congressmen reported last year that their mail was more in opposition to restrictive legislation than in support of it as had been the case in the past. Three years ago, nearly twice as many congressmen were proposing legislation as did in the past session. Such organizations as the American Medical Association, the American Heart Association and the National Paraplegia Foundation have initiated active programs in behalf of responsible laboratory animal utilization. A “task force” organized by the AMA includes representatives of the AMA, the American Hospital Association, the Association of American Medical Colleges, the Association of State Universities and Land Grant Colleges, the American Dental Association, the American Veterinary Medical Association and the National Society for Medical Research.

As we face the pressure for legislation of this kind in the 89th Congress, two questions should be asked. *First*, is there any reason to believe that the proponents of federal legislation will diminish their efforts or change their strategy of the past? There is no reason to entertain this thought. The

apparent effectiveness of the organized opposition to restrictive legislation suggests, however, that many legislators are better informed than in the past and, therefore, will not support actively, nor attempt to move legislation of an extreme nature. This does not mean, however, that they might not be led to support “moderate” legislation if sufficient pressure were exerted by their constituents. It is conceivable that some change in strategy by those who pursue this cause may come from attempts to introduce bills into state legislatures patterned after those that have failed to “move” in the Congress.

The *second* question can be directed to medical scientists. If medical scientists, in general, are opposed to federal regulation of animal experimentation, what constructive course do they propose and what evidence is there to show their intent to elevate standards of animal care? Biological scientists propose (a) to develop better methods of animal care through research, (b) to improve the level of animal care through education and training of laboratory personnel, (c) to disseminate new knowledge of animal needs and techniques for their care to other scientists, and (d) to provide for modern facilities for housing laboratory animals. The sophistication of modern medical research is such that precision in every parameter of experimentation, including that of the experimental animal, is essential if the validity of the results of research is to keep pace with the methods employed. New facilities for medical research and the renovation of existing facilities throughout the country are providing for increasingly improved standards for the storage and care of laboratory animals. Qualified veterinarians and biologists are supervising animal care facilities in medical schools and industrial laboratories. In 1963 the University of Illinois opened a two and one-quarter million dollar medical research building in which 13,000 animals are housed in constant temperature and controlled-humidity environment. Few human beings have better care. Granting agencies of the state and federal governments are defining standards of laboratory animal care in their contracts with universities.

As positive evidence of the intention of scientists to govern themselves is the establishment of the Animal Care Panel, an organization of institutions and individual scientists whose purpose is to improve the care and use of laboratory animals through a responsible program of education and

research. For example, a pilot study has been completed to test the feasibility of a program of voluntary accreditation of animal laboratories. Twenty-five institutions were selected, and a qualified representative inspected animal facilities at the time that the accreditation inspection of medical schools was held. Although the full report of this study has not been issued, the unofficial information available indicates that an accreditation program will have a far-reaching effect in elevating the standards of animal care. Two California scientists are associated with the Animal Care Panel in an official way: Doctor Orland A. Soave of Stanford University Medical School is president-elect of the Panel and editor of its journal, and Doctor Alfred G. Edwards of the Davis Campus of the University of California is a member of the board of directors.

One of the leading forces in behalf of responsible use of laboratory animals in teaching and research is the National Society for Medical Research. This organization was founded to improve public understanding of the principles, methods and needs of the biological and medical sciences. It has steadfastly maintained its opposition to and asserted its leadership against legislation which would restrict animal experimentation. The NSMR has been a point around which the total effort in behalf of medical science has been developed. It has maintained close contact with the legislative scene and can be relied upon to keep the biological community informed of developments. It is in a position to flash the signal when support from responsible citizens is needed to combat attempts to provide legislation that would be detrimental to medical research and teaching.

Above all, no greater support can be enlisted than that from individual physicians, veterinarians,

pharmacists, dentists and public health officials. By being alert to the dangers of governmentally restricted medical research and teaching, practitioners of the health professions in California can be the most essential force in this continuing vigil by advising their patients of their stake in upholding high standards of health and providing sound, effective, professional opinion to legislators if and when the occasion demands.

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**ADDENDUM:** The above analysis was prepared shortly after the adjournment of the 88th Congress late in 1964. During the first session of the 89th Congress, about 15 bills concerning the use and care of animals were introduced, some of them highly restrictive and punitive. Hearings were held by the appropriate subcommittee of the House Committee on Interstate and Foreign Commerce on 30 September 1965, at which time testimony, particularly that of supporters of the proposed legislation, was heard. Although bio-medical scientists were scheduled to testify on 1 October, the hearings for that day were postponed until early in the second session. At the time of this writing, the date for the postponed hearings has not been announced.

A second type of regulatory legislation for which hearings were held on 7 and 8 March 1966, by the House Committee on Agriculture is embodied in the Resnick (H.R. 9743) and Resnick-like bills. Legislation of this type would hamper medical education and research by restricting the procurement and transportation of cats and dogs to licensed dealers and licensed laboratories. This legislation would appear to eliminate public animal control agencies as a source of animals for legitimate educational and research purposes.

The current attitude of leaders in the scientific community is that, because of the persistence and pressure to which Congress has been subjected over the years, federal legislation of some type will be enacted during the second session of the 89th Congress. The big question is the kind of legislation that the Administration and the Congress will support. Of the regulatory bills that have been introduced to date, the Roybal bill is considered by scientists generally to be the least objectionable. The Administration is now known to have a bill for presentation during the second session, and early reports indicate that it can be supported by the educators and scientists as well as by members of the Congress.





# Post-Transfusion Hepatitis

## A Serious Clinical Problem

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■ *Serum hepatitis and infectious hepatitis may have a common pathogen and their few clinical differences the result only of a difference in portal of entry.*

*The risk of serum hepatitis from transfusions derived from prison and Skid Row populations is at least 10 times that from the use of volunteer donors. For every 100 patients receiving a single transfusion, the attack rate is 0.3 per cent when the donor is of the family or volunteer type and 3.2 per cent when the donor is from a prison or Skid Row population.*

*The most practical methods of reducing the hazard of serum hepatitis from blood are to limit the use of blood by giving one transfusion instead of two, two instead of three, etc., and especially by excluding, if possible, all prison and Skid Row donors.*

*It is urged that state and federal control of the quality of blood used for blood transfusions be studied with the possibility that measures may be taken to increase its safety. If it is necessary that blood from prison and Skid Row donors be used to meet the demands, such blood should be labeled as carrying a significantly increased hazard of transmitting serum hepatitis in order that the physician prescribing blood may take the necessary precautions.*

SERUM HEPATITIS is a clinical entity that may or may not be related to or caused by the viruses or family of viruses that cause infectious hepatitis. In many ways, the similarities between these two entities are so striking that the temptation is to consider their differences more a manifestation of portal of entry than of variances inherent in similar but not identical infectious agents. Perhaps they are.

The data contained in this review pertain to a 10-year study (1945-56) conducted at the University of Chicago Clinics. The number of patients

transfused with blood during that period was 12,598 and they received a total of 42,407 units of blood. This was a continuing study and some of the basic details are shown in Table 1. From an adjusted 21 per cent sample of these patients other studies were carried out and published elsewhere.<sup>1</sup> The study was completed before cardiac bypass procedures were instituted at that hospital.

### Epidemiology of Serum Hepatitis

*Age Distribution.* In most reports it is shown that approximately 85 per cent of cases of infectious hepatitis occur in patients under the age of 25. Because the infectious agent is ubiquitous, presumably there are many anicteric, asymptomatic cases of infectious hepatitis that are never

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TABLE 1.—*Blood Transfusions and Cases of Serum Hepatitis (1946-1956)*

Number of patients transfused*	12,598
Number of units of blood given	42,407
Average number of units per patient	3.4
Completeness of followup	92.0%
Number of observed cases: icteric serum hepatitis	189
Number of known deaths from serum hepatitis	21

\*Of these 12,598 patients, 11,627 are separate and independent patients in that they received no additional series (episodes) of blood transfusions during the period of study; 971 did have two or more series of transfusions.

diagnosed, and thus most people probably have some degree of immunity before the age of 25. In contrast, the majority of patients receiving blood transfusions are middle-aged or older, since the need for transfusion increases with age, as does the average number of transfusions given. For this reason, 75 per cent of the cases of icteric serum hepatitis were observed among patients over the age of 39 (Table 2).

*Sex Factor.* Sex of the patient does not influence the numbers of cases of hepatitis except that there are three sex-linked reasons for giving transfusions to female patients and one sex-linked reason for transfusions to males. These are childbirth, mastectomy and pelvic operations in women, most of which occur between ages 20 and 50. In males, prostatectomy is the sex-linked operation often requiring transfusion, and for the most part it is performed after age 50. When the cases of icteric hepatitis resulting from sex-linked reasons for transfusion are eliminated, the remaining numbers of cases of hepatitis are essentially equally distributed (Table 3).

*Incubation Period.* The length of incubation period has long been used as one method for distinguishing infectious hepatitis from serum hepatitis. It is true that jaundice develops within three

TABLE 3.—*Effect of Sex-Linked Indications for Blood Transfusion Upon Serum Hepatitis, by Age and Sex of Patients*

	All Cases	Sex-Linked Transfusions	Non-Sex-Linked Transfusions
Female	104	31	73
Male	85	4	81
Totals	189	35	154

*Age Distribution*

	0-19	20-49	50-59	60-69	70 and Older
Female	6	52	21	20	5
Male	6	21	26	23	9

to four weeks in most patients exposed to the pathogen orally. In serum hepatitis, jaundice may occur as early as the fourth week after transfusion and as late as the thirtieth week but three fourths of the cases occur between 30 and 90 days after transfusion, and half the cases occur before the sixtieth day (Table 4). These incubation periods are much shorter than they were originally thought to be, when cases occurring after the sixtieth day were arbitrarily considered serum hepatitis. The difference in length of incubation periods, while real, may not necessarily imply that two distinct infectious agents are involved. It may be that the variations in incubation time can be accounted for by the different portal of entry.

*Interrelationships of Serum Hepatitis and Infectious Hepatitis.* These things seem clearly established. First, that a fecal ultrafiltrate from a patient in the active stages of infectious hepatitis ingested by a susceptible person (Patient A) will result in a case of infectious hepatitis, usually within three to four weeks. If, however, this same filtrate is given parenterally to a susceptible person (Patient B), hepatitis of a variety similar to, if not identical

TABLE 2.—*Age Distribution, by Number and Per Cent, of Transfused Patients and of Patients Acquiring Icteric Hepatitis*

Age Groups	Number of Patients in Age Groups	Per Cent of Patients in Age Groups	Number of Cases of Icteric Hepatitis	Per Cent of Cases of Icteric Hepatitis by Age Groups
Under 1 year	642	5.1	2	1.1
1-9	768	6.1	3	1.6
10-19	516	4.1	7	3.7
20-29	1,423	11.3	7	3.7
30-39	1,959	15.5	29	15.1
40-49	2,365	18.8	37	19.6
50-59	2,431	19.3	47	24.9
60-69	1,828	14.5	43	22.9
70 and over	666	5.3	14	7.4
Total	12,598	100.0	189	100.0



TABLE 4.—*Incubation Period of Serum Hepatitis from Blood Transfusion*

	<i>Incubation Periods in Days</i>						<i>Total</i>
	<i>10-29</i>	<i>30-59</i>	<i>60-89</i>	<i>90-119</i>	<i>120-149</i>	<i>180-248</i>	
Cases among all patients transfused.....	4	78	54	23	15	15	189
Per cent of total cases by incubation period.....	2.2	41.1	28.7	12.0	8.0	8.0	100.0
Cases among patients when all transfusions given within one day.....	0	44	23	10	6	3	86
Per cent by incubation period.....	0	51.2	26.6	11.8	7.0	3.4	100.0
Cases among patients when all transfusions given within 3 days.....	2	57	29	13	8	4	113
Per cent by incubation period.....	1.8	50.4	25.6	11.4	7.1	3.7	100.0

with, serum hepatitis will develop in 30 days to six months. Second, Patient B, with the delayed form of hepatitis, even though his infection is derived from an ultrafiltrate of a primary case (Patient A) of infectious hepatitis, differs in that ultrafiltrates of his feces and urine, prepared during the active stages of his disease, will not induce hepatitis when given orally or parenterally to other persons.

However, if the blood or any of its icterogenic fractions from Patient A and Patient B are given parenterally to Patients C and D, both of these individuals, if susceptible, will in time have the delayed form of the disease—serum or transfusion-associated hepatitis. But, if the viremic blood from Patients A and B is administered orally, it will not produce hepatitis. It thus appears that the agent responsible for both entities is that which causes infectious hepatitis and that once this agent enters the bloodstream from the alimentary tract, it is in some way altered so that it is infectious only when administered parenterally. Nonetheless, the ultrafiltrates from the stool of Patient A remain infectious if administered orally.

It therefore appears that the virus of infectious hepatitis, once ingested, is readily transported from the alimentary tract to the circulation, but the agent, once in the bloodstream, does not return to the alimentary tract, at least not in a form that renders the stool infectious. Viremic blood apparently is infectious only when administered parenterally, not orally. It is also of interest that the blood of the patient with infectious hepatitis remains infectious long after the ultrafiltrate of his stool has lost its capacity to infect when given orally or parenterally. It appears therefore that the viremic "carrier" presented no problem until jennerian vaccination was introduced in 1798, a procedure which for 90 years entailed the preparation of the vaccine by harvesting and pooling the purulent lymph of people vaccinated with cow

pox. Once Copeman's method, in which the vaccine was cultivated on the skin of the calf, was introduced, the need for the human harvest disappeared and so did the occasional epidemic of jaundice associated with the jennerian-type vaccination.

With Ehrlich's introduction of a new treatment for syphilis in 1910, many of the epidemics of jaundice which followed were erroneously attributed to the heavy metals used, particularly his arsphenamines. (So abusive to Ehrlich were these criticisms that they may have contributed to his untimely death.) Not until 1942 was it generally recognized that these epidemics were due to the use of the multiple dose syringe and to improper sterilization of needles and syringes, although in 1920 Stokes had clearly indicated that jaundice associated with arsenical therapy was related to the blood of patients recovering from infectious hepatitis and was not caused by the drugs used.

The precautionary measures against viral hepatitis are of two kinds. One is strict isolation of the patient with infectious hepatitis until he has recovered clinically. No such measure is necessary for patients with serum hepatitis, although it may be advisable if the source of the infection is in question. However, in these latter patients, care must be taken to dispose of or to autoclave all equipment used for the drawing and testing of blood samples. The second precautionary measure relates to these persons when, after they recover from hepatitis, they wish to serve as blood donors. As such they are a potential source of infection to patients receiving their blood or its icterogenic products. At times the disease may be transmitted accidentally from viremic blood contained in syringes and glassware that may puncture the skin, as occasionally occurs among workers in blood laboratories. Aside from these general precautions, the use of gamma globulin is advisable, usually 5 to 10 ml on days 7, 21 and 35.<sup>1</sup>

## The Carrier-Donor

*Occult Carriers.* The viremic donor is the vector in serum hepatitis and, because his carrier state cannot be recognized by present laboratory methods, his menacing presence can only be determined when hepatitis develops in a patient receiving his blood and the diagnosis is reported to the blood bank, thereby identifying the donor, if suitable records are maintained. This carrier appears decidedly different from the patient recovering from viral hepatitis, whose viremic state lasts only for a few months to possibly a year or so.

The viremic carrier, whose blood is drawn at the blood bank and causes hepatitis when given to a susceptible patient, almost certainly has been carefully questioned and has reported that insofar as he knows he has never had this disease. Almost certainly in the case of the volunteer donor, the information he gives is correct and he is quite innocent of any knowledge that he has had hepatitis or that he has been a carrier of the virus. If, at this time, all practical tests of liver function were to be performed, the results would not differ from those in the normal population.\* Moreover, if one keeps such carriers under observation for years, icteric hepatitis appears not to develop later, yet their viremic state may continue indefinitely; if they serve as donors a second time some years later, their blood, when given to susceptible patients, may again result in cases of icteric hepatitis. It is possible that such a carrier may remain viremic for life, but he poses no threat to others if he is aware of his condition and does not serve as a blood donor, or if, in a physician's office or hospital, he is not given parenteral medication from a multiple-dose vial or syringe subsequently used, without proper sterilization, for inoculating other patients.

In short, the carrier who is so dangerous from the standpoint of transfusion appears to have established a state of indifference or tolerance to the virus and to be in good health, living in a completely compatible relationship with the organism. One can only speculate how such a harmonious coexistence can develop—from the standpoint of the host, as well as that of the virus. Several events which normally would occur, possibly in the carrier, do not. Ordinarily a virus replicates within the cell, often a specific cell. It continues this

process and as antibodies are formed the cellular structure is destroyed in the course of antigen-antibody reaction. Indeed, it is this reaction which appears to create symptomatic disease. When, however, no antibody is produced, the animal appears healthy and capable of living most if not all of its lifespan in this state of harmonious tolerance. The conditions under which this degree of tolerance has been established experimentally may not be the same conditions in which the carrier state is established in man, although they could be. In animals, the state apparently does not develop unless the species is infected late in the gestational period, or in the early prenatal period, before the animal is able to produce antibodies. This same mechanism possibly could occur in man and account for the carrier-donor, but we do not really know.

## Risk Rates of Contracting Serum Hepatitis from Blood

What is the probability that receiving a transfusion of a single unit of blood will cause icteric or clinically apparent hepatitis to develop in the patient? Several factors contribute. First, the evidence is clear that some icterogenic products are more virulent than others; that is, some will produce a higher attack rate than others. Thus a patient with some degree of immunity may not get icteric hepatitis from a product that causes jaundice in patients with less immunity. Therefore, the blood of a particular carrier may produce icteric hepatitis in one patient and not in another. Second, it appears that the proportion of susceptible patients is remarkably constant among similar population groups exposed to a common icterogenic agent. If exposed to a common agent of greater icterogenicity, this uniformity among subgroups is reflected throughout each group by an increase in the attack rates, as illustrated in Table 5.

Clearly, then, two important considerations which we know exist but cannot identify in relation to a specific donor or specific patient, are the degree of resistance of the patient and the degree of infectivity or virulence of the donor's blood. Only if the virulence of the carrier-donor's blood is sufficient to overcome the patient's resistance will a case of icteric hepatitis develop.

There are groups among donor populations whose blood produces more cases of icteric hepatitis than other groups. For example, the number of cases resulting from single transfusions when

\*Drug addicts and patients with chronic liver disease may have subacute and chronic states of viral hepatitis, in which case results of tests of liver function are usually abnormal and to some degree the patients may be symptomatically ill.



TABLE 5.—*Observed Attack Rates Among Isolated Subgroups of Normal Recipients of Aliquots from Common Lots of Pooled Ictericogenic Plasma*

<i>Number of Recipients in Subgroups</i>	<i>Cases of Serum Hepatitis</i>	<i>Attack Rates (Per Cent) in Subgroups</i>
<i>Lot No. 335</i>		
26	6	23.1
64	15	23.4
65	17	26.2
65	15	23.1
68	21	30.9
74	17	23.0
76	18	23.7
82	21	25.6
84	20	23.8
87	15	17.2
144	34	23.6
182	35	19.2
210	51	24.3
1,227	285	23.2
<i>Lot No. 338</i>		
63	8	12.7
70	11	15.7
75	12	16.0
76	8	10.5
80	13	16.2
85	11	12.9
449	63	14.0

the donors are of the prison-Skid Row variety is 10 times greater than the number of cases resulting when the donors are volunteers, members of the family or friends (Table 6). This difference is alarming, and it also obtains for multiple transfusions when the donor population is of the prison type. These results may seem striking; however, they have been confirmed by other investigators.<sup>2,3</sup>

One of two factors, or possibly both, would seem to explain this intolerable situation. It may be that the blood of the carrier-donor among the prison-Skid Row population is 10 times more virulent than that of the carrier who is a volunteer or family donor and thus overcomes resistance among patients 10 times more frequently than does the blood of the volunteer carrier-donor. Or perhaps

there are 10 times more carriers among the prison-Skid Row population than among the population at large.

### Practical Methods for Reducing the Risk

Two practical methods exist at this time whereby the numbers of cases of serum hepatitis from blood transfusions may be reduced. One is a method designed to reduce the attack rate for serum hepatitis by improving the quality of the donor populations used without necessarily reducing the numbers of transfusions given. The second is to reduce the number of units of blood to which each patient is exposed by extending the use of plasma volume expanders. It is essential to pursue both methods. To pursue one without the other will help, but the results will be much more impressive when both measures are actively pressed.

*Quality Control of Donor Populations.* From the information available to him, it is not possible under most circumstances for the physician prescribing blood for a patient to determine the quality of the population from which the donor comes.

Although most blood banks, as well as the American Red Cross, find it necessary at times to supplement their blood reserves by drawing blood from prison donors, unfortunately there is no indication on the label of the blood container informing the physician whether the blood comes from a high-risk donor population or from a low-risk volunteer group. Until it is required that such information be added to the label, the patient's physician cannot properly assess the risk the transfusion may carry. Without this information, it follows that the physician is unable to justify the extra precautionary measures that are necessary when a donor is from a high-risk group. In addition, when the source of blood is not known, the patient cannot be informed of the magnitude of the potential risk of hepatitis from the blood he is to receive.

TABLE 6.—*Number of Cases as Related to Source of Blood Transfused*

<i>Source of Blood</i>	<i>Total Number of Units</i>	<i>Number of Patients Transfused</i>	<i>Cases of Hepatitis Encountered</i>	<i>Number of Transfused Patients per Case of Hepatitis</i>	<i>Ratio of Units of Blood per Case</i>	<i>Average Number of Units per Patient</i>
All Prison .....	5,337	1,854	62	30	86	2.09
Some Prison .....	9,420	3,247	90	36	105	2.90
No Prison (all volunteer).....	27,650	7,497	27	278	1,024	3.69
Total .....	42,407	12,598	179*			

\*From blood purchased, and donors' source not known, an additional 10 cases of icteric serum hepatitis occurred, bringing the total number of cases to 189.

It is a curious fact that with quality control so much a part of the preparation of other biologic products, similar measures have not been taken by federal or state agencies to insure high quality of blood by insisting upon the use of high quality donor populations. This could be done either by the elimination of prison and similar high-risk donor populations or, as suggested above, if these must be used, to have the container in which the blood is supplied carry a special warning. With respect to most if not all other biologic products, state and federal laws require elaborate records to identify the source and quality of the product, its manufacturer and other simple but pertinent details in order that a particular lot or batch may be effectively traced. At present we cannot perform a practicable biological test on a particular unit of blood to detect the presence of a hepatitis virus which would make the unit unfit for transfusion. But we could be informed that the blood obtained from a high-risk donor population will yield approximately 10 times more cases of icteric serum hepatitis than blood derived from a low-risk population. Until the importance of such information is recognized and something is done to provide it, the physician cannot assume his proper role in prescribing blood—namely, to select, when possible, the safest product for his patient.

*Reduction in Number of Units of Blood Given per Patient.* Because multiple transfusions of blood carry all the risks of a single transfusion multiplied, any method that will safely permit the administration of fewer units of blood will to that extent reduce the patient's exposure risk to serum hepatitis. For example, two transfusions carry twice the risk of one and four transfusions carry essentially twice the risk of two, and so on. It thus becomes just as important to eliminate one transfusion in a patient who would otherwise receive two or three units of blood as it is to eliminate, when possible, the use of the single transfusion.

### Benefits of the Single Transfusion

In 1954 it was pointed out that a single transfusion carried a hazard greater than was generally appreciated; and in the particular instance then being discussed, serum hepatitis, which had developed approximately seven weeks after the infusion of one unit because of a transient episode of hypotension during appendectomy under spinal anesthesia, had caused the patient's death. Since a single transfusion was all that was necessary, would

not another fluid with less hazard have been adequate in this patient? As to this particular case, the answer is self-evident.

Unfortunately what appeared in retrospect to have been the abuse of the single transfusion in this instance caused many investigators to generalize that all single transfusions were unwarranted. It has been distressing to learn that the Joint Commission on the Accreditation of Hospitals has included in its questionnaire an item regarding the number of patients receiving single transfusions, without inquiring as to the number of patients receiving two or three transfusions. The intent of this question has been misinterpreted, because, upon making inquiries in a number of hospitals in this state and elsewhere, the author learned that the trend is for administrators to exert pressures to curtail the number of patients receiving a single transfusion, with the result that some physicians admit that, to minimize criticism, it is easier to give two or three units than one. Any attempt to reduce the hazards of blood transfusions is laudable, but an attempt such as this one appears to enlarge the problem rather than to reduce it. Much more can be accomplished, however, if blood from a high-risk carrier population be labeled as carrying an increased hazard of serum hepatitis. Single transfusions from the family donor will cause approximately three cases per thousand patients, whereas those from the high-risk population carry a risk of 32 cases per thousand.

The effect of reductions in numbers of blood transfusions upon an actual series of patients transfused is illustrated in Table 7. If it were possible to eliminate one transfusion from each of the 12,598 patients transfused with blood, the total transfused would be reduced by 37.6 per cent, or by 4,738 patients. Of the remaining 7,860 patients, 3,030, or 38.5 per cent, would now receive one transfusion instead of two. Were it possible to eliminate two transfusions from every patient transfused, the number of patients receiving blood would be reduced from 12,598 to 4,830, and the number receiving a single transfusion under these conditions would be 1,561 or 32.0 per cent of the total 4,830 now exposed.

With this reduction in the number of blood transfusions administered per patient, the total number of units of blood given would be reduced by scarcely 20 per cent, whereas the total number of patients exposed to blood would be reduced by more than 60 per cent who thereby would be



TABLE 7.—Effect of the Elimination of One and Two Transfusions in a Patient Population in a General Hospital

	Number of Transfusions						Total
	1	2	3	4	5	6 and more	
No. patients transfused .....	4,738	3,030	1,561	964	574	1,731	12,598
Per cent patients transfused.....	37.6	24.0	12.4	7.7	4.6	13.7	100.0
No. cases of hepatitis.....	21	48	26	21	17	46	179
No. patients transfused if first transfusion were eliminated .....	3,030	1,561	964	574	5 and more 1,731		7,860
Per cent patients transfused.....	38.5	19.9	12.3	7.3	22.0		100.0
No. cases of hepatitis.....	48	26	21	17	46		158
No. patients transfused if first two transfusions were eliminated.....	1,561	964	574	4 and more 1,731			4,830
Per cent patients transfused.....	32.0	20.0	12.0	36.0			100.0
No. cases of hepatitis.....	26	21	17	46			110

Note: The benefits shown in this table are the results of the elimination of one and two units of blood in patients receiving only one or two units and therefore avoiding blood exposure entirely. No attempt was made to adjust for benefits derived when the first two transfusions are deleted from those receiving three or more units of blood.

spared any risk of serum hepatitis. With these reductions the 69 cases that occurred among recipients of one and two units of blood would have been avoided and probably an additional but indeterminate number would not have occurred among those receiving larger numbers of transfusions.

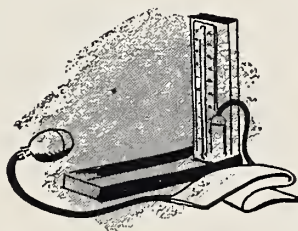
It can be seen from the above that when blood is used conservatively, and when this conservatism is applied to multiple as well as single-unit recipients, the proportion of single transfusions given in any general civilian hospital will remain at approximately 35 per cent of all transfusions given, excluding blood used for extracorporeal circulation. By use of expanders, properly selected and appropriately administered, the use of blood in

many patients now receiving two or even three units could be avoided.

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# Medical Staff Conference

## Hypertrophic Subaortic Stenosis

*These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.*

DR. DOUGLASS C. TORMEY:\* The patient is a 27-year-old married Caucasian woman now in her third admission to the University of California Hospitals. Her chief complaint is increasing difficulty in breathing. For as long as she can remember the patient has experienced easy fatigability and inability to keep up with her peers. At age 17, she noted the first of occasional episodes of paroxysmal nocturnal dyspnea. During her first pregnancy at age 19, mild symptoms of congestive heart failure developed. These recurred during her second pregnancy at age 19. At this time, she also experienced symptoms resembling those of angina pectoris. In the postpartum period, she continued to experience wheezing and shortness of breath and was told she had asthma. Since that time, she has noted gradually increasing exertional dyspnea, orthopnea (requiring three pillows), and angina pectoris unrelieved by nitroglycerine. She has never fainted or had leg cramps.

In September 1965, the patient entered the University of California Hospitals for the first time for cardiac evaluation. She was alert and cooperative, but anxious. Blood pressure was 124/70 mm of mercury; pulse, 80 and regular; respirations, 16 per minute; temperature normal.

Pertinent abnormal findings on physical examination were confined to the cardiovascular system and included a moderately slowly rising carotid pulse which rapidly fell off. Neck veins were flat. The left border of cardiac dullness and point of maximum impulse were 11 cm from the midsternal line in the sixth left intercostal space. There was a double impulse at the apex and a systolic thrill at the left sternal edge at the fourth interspace. A grade IV/VI harsh systolic ejection mur-

mur was audible over the entire precordium and radiating into the neck and axillae but was loudest at the left sternal edge at the fourth interspace. It started after the first heart sound and ended before the second heart sound, except at the apex, where it obscured the second heart sound. The aortic second sound was greater than the pulmonic second sound. No gallop or pericardial rub was heard. Peripheral pulses were of the same quality as the carotids. There was no abdominal organomegaly. Slight pretibial edema was present.

Laboratory findings included: routine complete blood cell count and urinalysis and creatinine determination were within normal limits. An electrocardiogram was consistent with considerable left ventricular hypertrophy and a combined ventricular conduction defect. A phonocardiogram showed rapid upstroke of the carotid tracing with a mid-systolic dip and a systolic ejection murmur, loudest at the apex. X-ray films of the chest were felt to be most compatible with combined mitral stenosis and insufficiency.

The patient underwent cardiac catheterization on 8 September 1965. The results of these studies and the serial angiocardiogram were compatible with the diagnosis of idiopathic hypertrophic subaortic stenosis. In view of the progressive clinical symptoms and the diagnosis of idiopathic hypertrophic subaortic stenosis, the patient was readmitted at this time for a trial of treatment with propranolol.

DR. LLOYD H. SMITH, JR.:† We are very pleased to have Dr. Eugene Braunwald here this morning to lead the discussion. Dr. Braunwald received his undergraduate and medical training at New York

\*Resident Physician in Medicine.

†Professor of Medicine and Chairman, Department of Medicine.



University, graduating with honors in 1952. Following this, he took his internship at Mt. Sinai Hospital. Hypertrophic subaortic stenosis, is another area in which and then early in his career he indicated the direction of his interest by taking a fellowship in cardiopulmonary physiology at Columbia. From there, he went to the National Heart Institute with which he has been associated ever since, except for a period of further residency training at Johns Hopkins. He has been Chief of the Cardiology Branch of the National Heart Institute for the last five years. Dr. Braunwald and his associates have won international recognition for their outstanding contributions in cardiology, particularly in the general area of human cardiovascular pharmacology and physiology. Our topic for discussion today, hypertrophic subaortic stenosis, is another area in which this productive group has made contributions. We are delighted, therefore, to have Dr. Eugene Braunwald with us today.

DR. EUGENE BRAUNWALD:‡ About eight years ago, we studied a 17-year-old boy in whom we

‡Chief, Cardiology Branch, National Heart Institute, National Institutes of Health, Bethesda, Maryland.

made the diagnosis of discrete congenital membranous subaortic stenosis. At left heart catheterization, the typical finding of a pressure drop in the outflow tract of the left ventricle was demonstrated. The patient was symptomatic and operation was recommended. At open heart operation, carried out by Dr. Morrow§ with the aid of potassium arrest, there was no obstruction evident either in the aorta or in the left ventricle. We had no way of explaining this extraordinary occurrence and fortunately the patient recovered. Two weeks later an almost identical sequence of events occurred, and again we were extremely embarrassed by the findings at operation. We began then to appreciate that we were dealing with a condition that had not been recognized previously and began to re-examine the clinical and hemodynamic syndrome in these two patients. At about the same time, Sir Russell Brock reported a somewhat similar experience in England, and soon it became apparent that a group of patients existed who had a form of obstruction to left ventricular outflow which was produced by tremendous hypertrophy of the left

§Andrew G. Morrow, M.D., clinical center, National Institutes of Health.

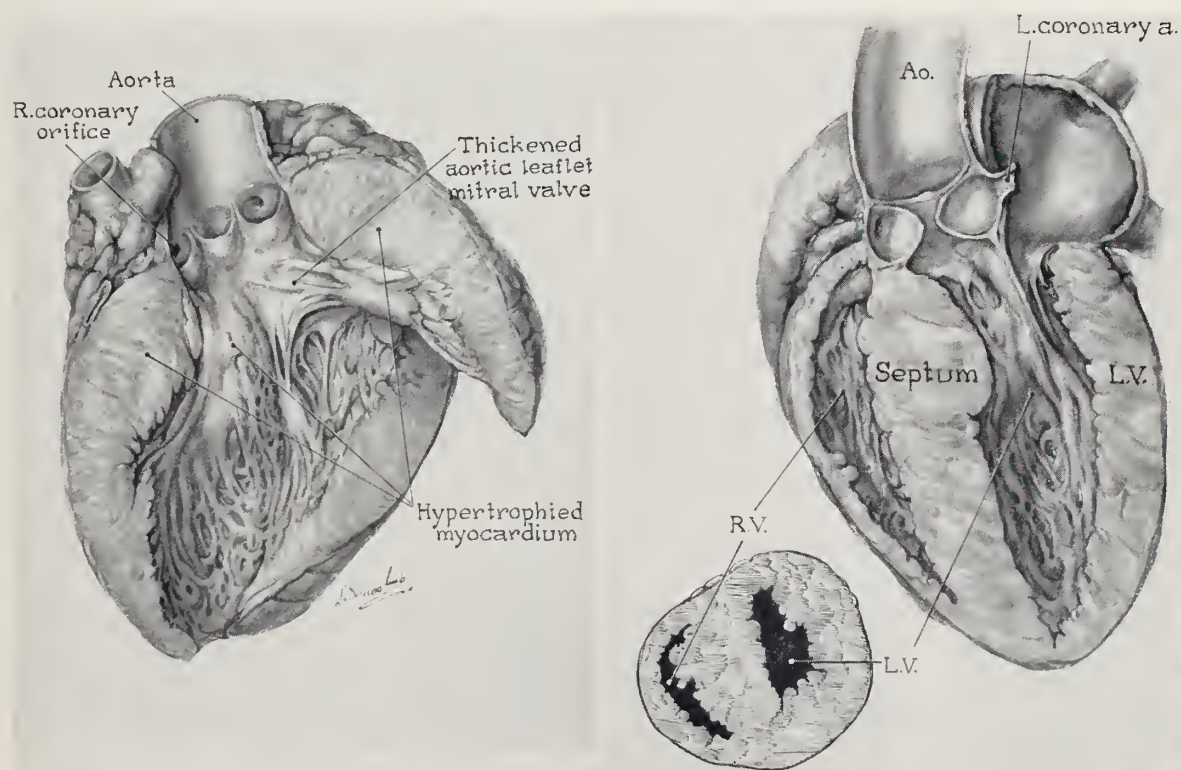


Figure 1.—Left, drawing of left ventricular wall and cavity of a patient with idiopathic hypertrophic subaortic stenosis; Right, sagittal and coronal sections showing disproportionate thickening of the ventricular septum encroaching on the two ventricular cavities.

ventricular muscle and particularly of the interventricular septum which encroached upon the left ventricular outflow tract. This has proved to be a very common form of obstruction to left ventricular outflow, much more common than congenital discrete subaortic stenosis. We have the impression that this is a relatively common form of heart disease, and have had the opportunity to study 106 patients with idiopathic hypertrophic subaortic stenosis (IHSS) in the past seven and a half years at the National Heart Institute. I would like to summarize our general impression of this interesting condition.

Figure 1 is drawings of the heart of a patient with IHSS. There is tremendous hypertrophy of the entire left ventricle, with bulging of the ventricular myocardium in the septal region, several centimeters below the aortic valve, and the ventricular cavity is relatively small. There is also bulging of the septum into the right ventricular cavity. On coronal section, the ventricular cavities appear as mere slits.

It is quite clear now that a number of conditions are probably lumped together under the general heading of IHSS. First of all, the patients can be clearly divided into those with and those without a family history of this disease. We have the distinct impression from our analysis of the family histories that in the 30 to 40 per cent of patients in whom this disease is familial, it is transmitted as an autosomal dominant characteristic; males and females are equally frequent among the patients with a family history. On the other hand, the male to female ratio among the patients without a family history has been four to one. The ages of patients have varied between five and 65 years with the majority in the third and fourth decades. The most frequent symptoms are exertional dyspnea and angina pectoris. Dizziness is also very common, especially on assuming the erect posture. Paroxysmal nocturnal dyspnea occurs in about a third of the patients. Syncope, fluid accumulation and palpitations occur less frequently.

Now, what can we expect from clinical examination? I indicated that among the nonfamilial groups the males predominated, and we are struck by the fact that many of these have a history of unusual athletic achievement and are quite muscular. I'm not quite sure what that means, but it may be related in some fashion to the hyperkinetic heart syndrome which Dr. Richard Gorlin has

described. On superficial examination of the patient with IHSS, one would not think of obstruction to left ventricular outflow. The findings in general suggest ventricular septal defect or mitral regurgitation. The most common features on physical examination are a left ventricular lift, a double apical impulse, and a thrill along the lower precordium. I emphasize that the thrill is not usually felt along the carotid vessels, but rather over the lower precordium and at the apex. The pulses are brisk, and very frequently an atrial sound is heard. The systolic murmur is most prominent at the apex and along the left sternal border and is usually not well transmitted to the neck. The second heart sound often splits paradoxically, that is, the aortic component follows the pulmonic component. A diastolic murmur along the left sternal border, that is, a murmur of semilunar valve incompetence, is extremely unusual in IHSS.

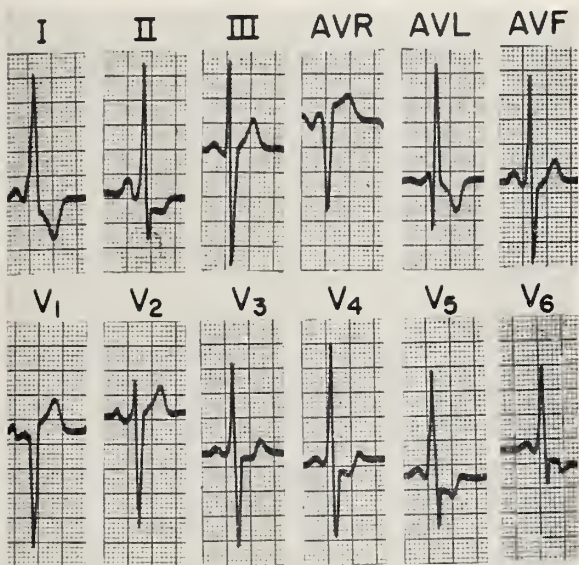
It is important to consider some of the features that differentiate IHSS from valvular aortic stenosis. The systolic thrill and murmur in IHSS are most prominent along the left sternal border and at the apex, whereas in valvular aortic stenosis they are most obvious at the base of the heart with radiation to the jugular notch and along the carotid vessels. In IHSS, the characteristic systolic murmur is usually ejection in type, sometimes holosystolic, and is usually medium pitched. In valvular aortic stenosis it is always an ejection murmur and is generally lower pitched and rasping. A systolic ejection sound is unusual in IHSS; it is common in valvular aortic stenosis, particularly in the absence of valvular calcification. A diastolic blowing murmur of semilunar valve incompetence heard along the sternal edge is very unusual in IHSS and is relatively common in the patients with aortic valvular disease. In IHSS, the arterial pulse rises rapidly and is bifid (*bisferiens*). In valvular aortic stenosis, it is anacrotic and tends to rise slowly. In IHSS, both on auscultation and by phonocardiography, a very prominent fourth heart sound is frequently evident, and there is generally a pause between the first sound and the onset of the murmur; this pause probably results from the fact that there is very little obstruction early in systole. The apex cardiogram shows a double impulse and the first component of the double impulse is usually synchronous with the fourth heart sound.

All of these findings suggest increased activity of the atrium in IHSS. These findings are tied in with an interesting clinical feature. When patients



with IHSS lose their atrial contribution to ventricular filling—that is, when they develop nodal rhythms, atrial fibrillation or flutter—their circulatory state deteriorates quite rapidly. Fortunately, these arrhythmias are not very common but when they occur they may be true emergencies.

In IHSS the carotid pulse rises sharply and then falls during midsystole. There is a plateau or secondary elevation during late systole and the incisura is often delayed. The jugular venous pulse shows a prominent “a” (atrial contraction) wave. The electrocardiogram is also helpful in the diag-



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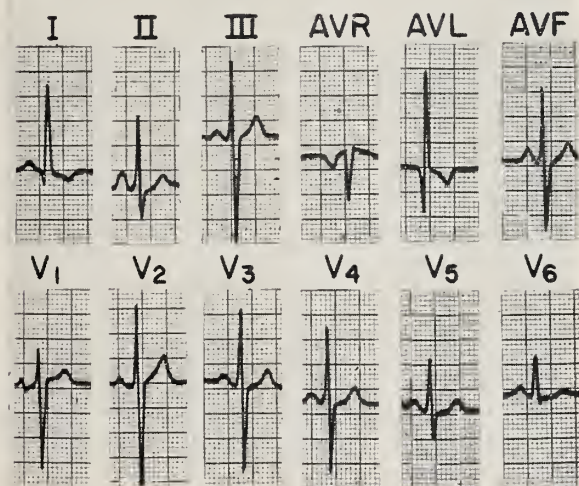


Figure 2.—Intermittent Wolff-Parkinson-White electrocardiographic configuration in idiopathic hypertrophic subaortic stenosis. This pattern is present in the tracing at the top but is absent in the tracing shown at the bottom which was from the same patient 10 months later.

nosis. In most instances it shows evidence of left ventricular hypertrophy but there are two other important findings. One of these is the Wolff-Parkinson-White (WPW) syndrome (Figure 2). In many patients the electrocardiogram resembles but is not entirely typical of the WPW configuration in that it has two of the three components of the triad, a short P-R interval and slurring of the R wave—that is, a delta wave. QRS prolongation is seen less commonly. Another interesting electrocardiographic feature is the presence of abnormal Q waves in the electrocardiogram, as observed in the tracing of the patient who was presented this morning. Most commonly very deep, broad Q waves are found in leads II, III, and aVF, and over the left precordium (Figure 3). As a matter of fact, several of our patients were referred because they were suspected of having asymptomatic coronary artery disease. However, the abnormal Q waves are not produced by myocardial infarction, but are probably related to the tremendous septal hypertrophy which exists in IHSS.

The chest roentgenogram is less helpful diagnostically, since the cardiac silhouette may be quite variable. It may be perfectly normal or there may be considerable cardiomegaly. In general, the left ventricle appears to be most prominent and the aorta is rarely dilated; no calcium is seen in the region of the aortic valve on fluoroscopy.

The directly recorded brachial arterial pulse is distinctly helpful diagnostically. The pressure rises very rapidly, falls, and often shows a second elevation before the diastolic notch. If the rate of the pressure rise is recorded, it is found to be distinctly accelerated in the majority of patients with IHSS. The withdrawal pressure tracing at the time

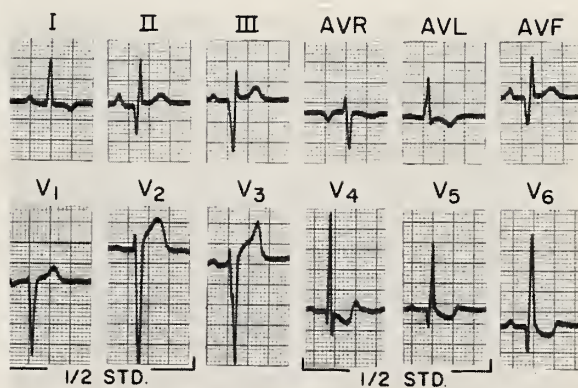


Figure 3.—Electrocardiogram showing abnormal Q waves in leads II, III, aVF, V<sub>5</sub> and V<sub>6</sub>. The precordial leads exhibit the voltage criteria for left ventricular hypertrophy.

of left heart catheterization then is helpful in localizing the obstruction to the subvalvular region. The angiocardiograms are also helpful in the diagnosis. In the lateral view, the left ventricular cavity is very small, almost completely obliterated in systole by the hypertrophied muscle. The left atrium may be enlarged, particularly when mitral regurgitation is present; the latter complication occurs in about one-third of all patients with IHSS. It probably results from distortion of the mitral valve produced by the greatly enlarged interventricular septum.

The aspect of IHSS which has interested me the most is the variability of obstruction. We became aware of this phenomenon in the following way. In 1958, we were studying the effects of acute digitalization on left ventricular hemodynamics in patients with valvular aortic stenosis, and came across a patient whom we believed to have valvular

aortic stenosis. I went to see her the evening before the procedure and explained to her that we planned to measure her intracardiac pressures and to study the effect of digitalis. She said, "Oh no you won't, I won't sign permission. I know that I have a big heart and heart disease, and wherever I go the doctors want to give me digitalis and whenever they do this, I get worse. The last time this happened I almost died. You can do whatever you like but you can't give me digitalis." We respected her wishes, and at the time of the hemodynamic study found that she had IHSS. In view of her history of digitalis intolerance we studied the acute effects of ouabain, a rapidly acting glycoside, in other patients with IHSS. In all instances the obstruction became more severe following the drug, and usually when given orally digitalis exaggerates many of the symptoms of IHSS.

Isoproterenol is another agent which helps

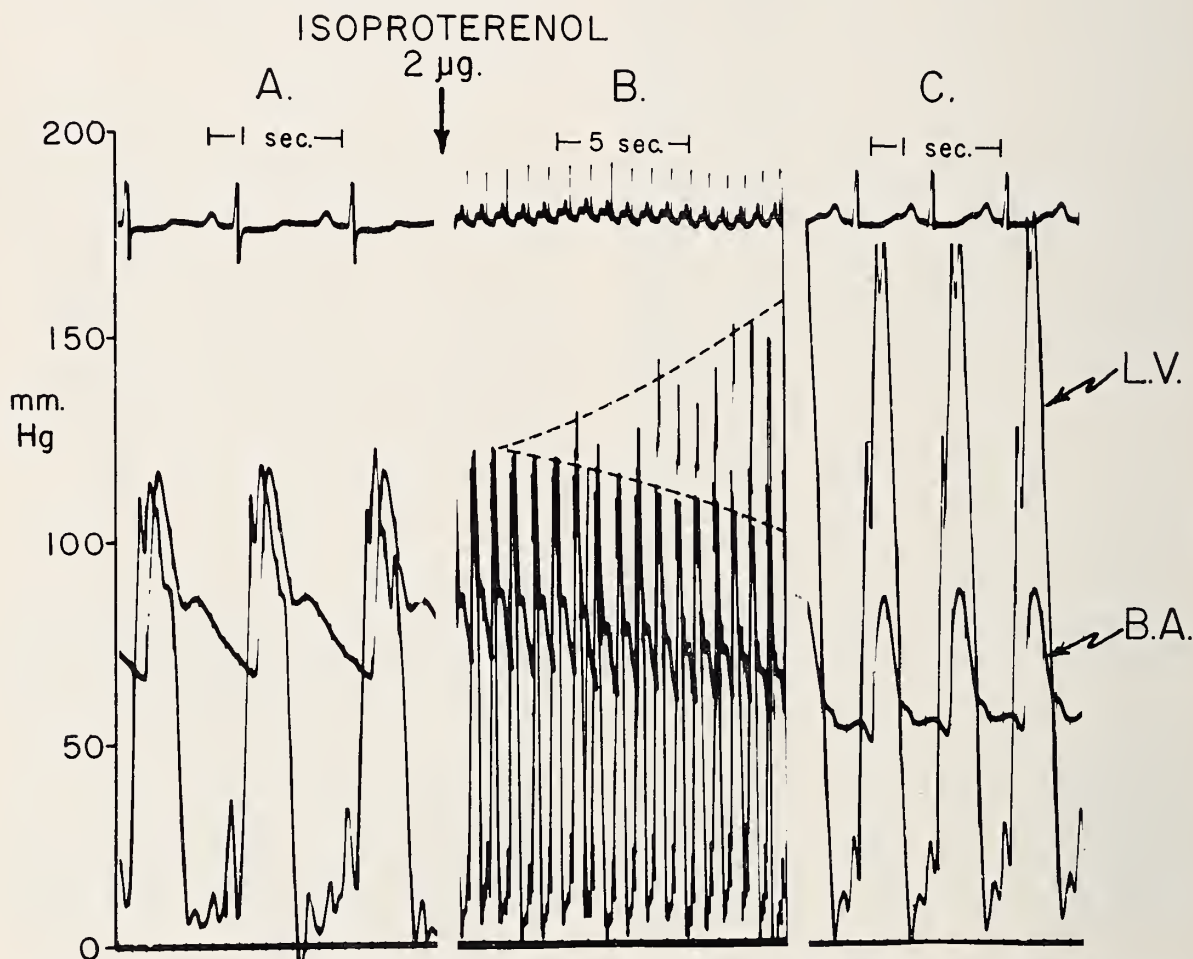


Figure 4.—Simultaneous pressures recorded in the left ventricle (L.V.) and brachial artery (B.A.) before and immediately after intravenous injection of 2 µg of isoproterenol in a patient with idiopathic left ventricular hypertrophy without obstruction in the resting state. The broken lines indicate the fall in B.A. pressure and the simultaneous elevation of the L.V. systolic pressure—that is, the development of severe obstruction to left ventricular outflow.



many patients with heart disease but which has the opposite effect in IHSS. Isoproterenol is a powerful myocardial stimulant, but in patients with IHSS it may increase the pressure gradient and lower the cardiac output. As a matter of fact, in patients with idiopathic myocardial hypertrophy without any hemodynamic evidence of obstruction, the administration of isoproterenol may precipitate severe obstruction (Figure 4). Now if isoproterenol, a beta adrenergic stimulant, intensifies the obstruction, what would a beta adrenergic blocking drug do? Well, these drugs have very little hemodynamic effect in patients in the resting state, suggesting that there is probably little activity of the cardiac sympathetics at rest. On the other hand, beta blocking drugs certainly can prevent or at least diminish the intensification of obstruction which occurs during muscular exercise, during anxiety or during an infusion of isoproterenol. Methoxamine, an alpha adrenergic stimulator with little or no direct cardiac effects, has an effect which is opposite to that of isoproterenol and reduces or eliminates obstruction.

Another situation in which the obstruction varies is simple changes of body position. Raising the legs may remove the gradient. Recently, we have placed patients on a tilt table and have found a decided intensification of the obstruction with tilting into the upright position. Similarly, during the Valsalva maneuver, at a time when blood flow through the left ventricular outflow tract is diminishing, the gradient increases; and after the release of the strain, the gradient decreases or even disappears transiently. This reaction is the opposite of the one observed in patients with valvular aortic stenosis. Nitroglycerin is another drug which has a paradoxical effect and increases the obstruction in patients with IHSS.

Can we develop a unifying concept from all of these diverse observations? I think that any influence that tends to reduce the systolic volume of the left ventricle and lowers the distending pressure in the left ventricular outflow tract increases the obstruction in patients with IHSS. The systolic volume of the ventricle can be reduced by an inotropic influence like digitalis; it can be reduced by diminishing blood flow into the heart, as in the Valsalva maneuver or during head-up tilting, and it can be diminished by lowering arterial pressure so that the ventricle empties more readily, as occurs with nitroglycerin. Dr. Oakley and her colleagues at Hammersmith Hospital in London have

shown that intensification of obstruction occurs with blood loss, resulting in a fall in arterial pressure, decreased venous return and an increase in heart rate. All of these effects would act in concert to make the ventricle smaller. Muscular exercise has a similar effect.

Any influence that makes the heart larger during systole or increases the distending pressure in the outflow tract tends to reduce obstruction. General anesthesia accomplishes this by reducing the sympathetic drive to the heart and by exerting a negative inotropic effect. Methoxamine increases arterial pressure, and diminishes heart rate—both of these tend to increase the size of the ventricle during systole. Beta adrenergic blockers reduce obstruction by blocking the positive inotropic influences of the sympathetic nervous system. Clamping the aorta has an effect very similar to that of methoxamine. Induced hypervolemia or tilting into the head-down position tends to increase venous return, increases the volume of the left ventricle during systole and tends to diminish the obstruction.

Now as to therapy. Digitalis should be discontinued in patients with IHSS, with the exception of those with atrial fibrillation and a rapid ventricular response and possibly patients with mild obstruction but severe heart failure. Nitroglycerin, isoproterenol and vigorous diuresis should be avoided. In an emergency, assumption of the "shock" position with the head lowered and the legs elevated, as well as the infusion of phenylephrine or methoxamine, is helpful in relieving obstruction. Together with Dr. Lawrence Cohen we are currently evaluating the beta-adrenergic blocking agent propranolol (Inderal®) in the conservative management of IHSS. At this time we have the distinct impression that the drug may be particularly helpful in relieving angina pectoris and it may prove helpful in selected patients in whom angina pectoris is the most prominent symptom.

As I indicated earlier, we have now studied in some detail 106 patients with IHSS. However, we have recommended operation for only 19. I think that this relatively low percentage reflects our lack of enthusiasm for operation, for we are dealing with a diffuse myocardial disease. IHSS is a cardiomyopathy of the hypertrophic type and obstruction to ventricular outflow is only one component of this disease. It is now clear that while the obstruction can be relieved surgically, the most that we can hope to achieve with operation is to con-

vert a patient with IHSS and severe obstruction to one who has idiopathic left ventricular hypertrophy without obstruction. The operative procedure employed by Dr. Morrow consists of opening the ascending aorta, retracting the aortic valve leaflets, and incising the bulging hypertrophied muscle in the ventricular septum. This procedure is reminiscent of the Ramstedt operation for pyloric stenosis in which the contraction ring is incised. In about half of the patients Dr. Morrow hasn't removed any muscle at all but has just made a very deep incision and extended it with blunt dissection; in the other patients the amount of myocardium removed has been small.

What has happened to these patients? Nineteen patients have been operated upon and 18 are living. One died of arrhythmia about a week after operation. The hemodynamic results have been quite good, and all but one of the patients have shown considerable clinical improvement as well. However, their heart size has not diminished and they still manifest considerable evidence of pronounced left ventricular hypertrophy. Our current criteria for recommending operation include: (1) relatively serious clinical disability (functional Class III or IV according to the New York Heart

Association); and (2) hemodynamic evidence of relatively serious obstruction to left ventricular outflow, with an intraventricular pressure gradient exceeding 60 mm of mercury.

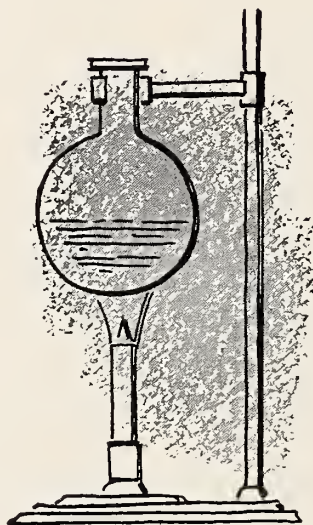
DR. LLOYD H. SMITH, JR.:\* I would like to thank Dr. Braunwald for this superb discussion. I am afraid that our time has gotten to the point that we cannot have public questioning.

\*Professor and Chairman, Department of Medicine.

## HYPERTROPHIC SUBAORTIC STENOSIS

### Recent Summaries in the Literature

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# CASE REPORTS

## Benign Tumor of the Common Bile Duct

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JOHN H. WINKLEY, M.D., *Reseda*

BENIGN TUMORS of the extrahepatic biliary ducts, exclusive of the gallbladder, are extremely rare. Our experience with this condition during choledocholithotomy prompted this case report.

### Report of a Case

A 65-year-old white woman was admitted to the Kaiser Foundation Hospital, Los Angeles, with complaint of intermittent colicky pain in the right upper quadrant of the abdomen of three weeks' duration. Three days before admission, the patient noticed that her skin was yellow, urine dark and stools clay colored. There was no previous history of gallbladder disease. The patient had been treated for hypertension for the previous five years.

She was obese, slightly icteric and appeared not to be in distress. Blood pressure was 170/100 mm of mercury, pulse rate 80 and temperature 98.4°F. Tenderness was noted on deep palpation of the right upper quadrant of the abdomen. No mass was felt and the liver, spleen and gallbladder were not palpable.

Hemoglobin was 14.2 gm per 100 ml and leukocytes numbered 11,500 per cu mm with normal differential. Urinalysis was positive for bile but otherwise not remarkable. Serum glutamic pyruvic transaminase was 75 units and alkaline phosphatase was 36.4 Bodansky units. Total bilirubin was

3.3 mg per 100 ml with 1.6 mg direct fraction. Prothrombin time was 105 per cent.

On radiological examination no abnormalities were seen in the chest and the gallbladder was not visualized on a cholecystogram. Studies of the upper gastrointestinal tract and the small bowel were within normal limits.

A diagnosis of cholelithiasis with obstructive jaundice was made and laparotomy was done through a right subcostal incision. The gallbladder, thickened and tense, contained numerous small calculi. The cystic duct was patulous and there was a calculus near its junction with the common bile duct. Also a calculus about 5 mm in diameter was impacted in the ampullary region of the common bile duct. The duct was slightly enlarged—12 mm in diameter. No other abnormality was noted on careful palpation of the liver, pancreas, stomach, duodenum and kidneys.

Following cholecystectomy the supraduodenal portion of the common bile duct was incised and the calculus was easily removed. At this point, a pedunculated polyp 1 cm in maximum diameter was seen projecting into the lumen of the common bile duct, just distal to the junction of the cystic duct. The pedicle was 5 mm in diameter. Although the polyp almost filled the lumen, it did not occlude it completely. Through an elliptical incision in the common bile duct, the polyp and about 0.5 cm of duct wall on either side of it were removed. On frozen section examination, no malignant change was seen. The common bile duct was then repaired over a T-tube. A cholangiogram showed no other pathologic change in the biliary tree.

The postoperative course was smooth and the patient was discharged on the eighth postoperative day. She was then asymptomatic, anicteric and having normal bowel movements. The T-tube was left in place until the twenty-first postoperative day, then removed when a cholangiogram showed no abnormality and serum bilirubin was within normal limits. When last seen, 18 months after

From the Southern California Permanente Medical Group and Kaiser Foundation Hospitals, Los Angeles.  
Submitted 14 September 1965.

operation, the patient was well. On microscopic examination of a section of the tumor (Figure 1) it was described as a benign polypoid adenomatous growth.

## Discussion

The literature on benign tumors of the extrahepatic bile ducts is scanty. In 1950, Chu<sup>4</sup> reviewed the reported cases and added one of his own. At that time only 30 cases were well documented. One more was reported by Anderson and coworkers.<sup>1</sup> In 1962, Dowdy and coworkers<sup>5</sup> reported three more cases, and on reviewing the literature from 1950 to 1960 they found reports of 40 additional cases. Also in 1962 Cattell and coworkers<sup>3</sup> reported nine cases.

Chu estimated that benign tumors can be expected in one out of five thousand operations on the biliary tract. However, some autopsy studies indicate a much higher incidence and suggest that the lesions are often overlooked. They occur in both sexes equally and at all ages but with prevalence in the sixth decade of life. In about one-third of cases the lesions are located at the ampulla of Vater. Usually they occur singly but in four cases multiple tumors were reported—all papillomas. Although widely variable in size, usually the tumors are 1 to 3 cm in diameter.

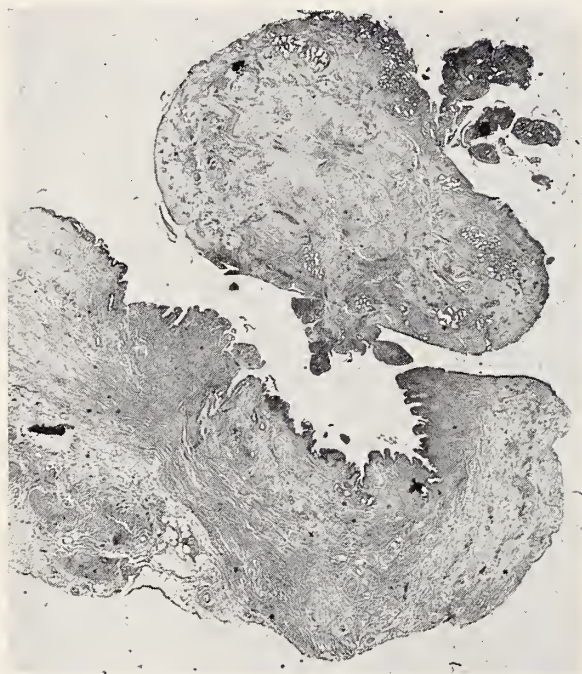


Figure 1.—Photomicrograph of resected specimen showing the polyp and the excised segment of the common bile duct ( $\times 15$ ).

The largest tumor ever reported weighed 750 gm.

The growth may be sessile or pedunculated, soft or firm; and usually it projects into the lumen of the duct.

Histologically, the commonest types are the papillomas and adenomas. The former most commonly occur at the ampulla and the latter elsewhere in the biliary tract. The cause is unknown. Lipomas, carcinoid tumors, hamartomas, leiomyomas, granular cell myoblastoma and various other types have been reported. Cattell<sup>3</sup> considered the papillary tumors premalignant.

Surprisingly, the incidence of simultaneous choledocholithiasis is low. Stones were present in four cases of 52 reviewed by Moore.<sup>6</sup> Dowdy and coworkers<sup>5</sup> said that in five out of 43 cases reported between 1950 and 1960 there were calculi in the common duct.

In the case herein reported it is evident that the calculus, not the tumor, was the cause of jaundice.

Clinically, preoperative diagnosis is very difficult. Symptoms are widely variable and usually they develop gradually, sometimes over many years but occasionally in a few weeks. The incidence of various subjective symptoms is as follows: jaundice in 90 per cent of cases, pain in 81 per cent, dyspepsia in 42 per cent, weight loss in 42 per cent, chills and fever in 28 per cent and hemobilia in 10 per cent.<sup>5</sup> In most patients the liver is enlarged. If the tumor is below the opening of the cystic duct and causing obstruction, the gallbladder is usually enlarged and palpable. Rarely the tumor itself is palpable.

Radiological examination is occasionally helpful. In four reported cases the lesion was suspected from observations on intravenous cholangiography. One should suspect the tumor in cases of obstructive jaundice in which a cholecystogram shows no abnormality and symptoms recur after cholecystectomy. Even at operation diagnosis may be very difficult, for the tumors are often small and soft and probes may be passed through and around them. Operative cholangiography and careful palpation are very helpful. Duodenotomy is essential if ampullary tumor is suspected.

The treatment of choice is local excision; there is no place for radical procedures. Up to 1950, only 20 per cent of cases were successfully treated; from 1950 to 1960, 75 per cent. In this same period, the tumor was first noted at au-



topsy in six of the total of 43 cases, and in four of these six the patient had had biliary operation not long before death. Operative mortality in the 1950-1960 period was 10 per cent.

## Summary

The case of a 65-year-old woman with a benign adenomatous polyp of the common bile duct is presented. The lesion was discovered incidentally during exploration of the common duct for an impacted calculus. Both the tumors and the stone were removed successfully.

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# Occipitalization of Atlas With Hypoplastic Odontoid Process:

## *A Cineradiographic Study*

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BERNARD S. STONE, M.D.

GREGORY BARD, M.D., *San Francisco*

CONGENITAL ANOMALIES at the craniovertebral articulations and in the high cervical area have been of interest, neurologically and roentgenologically, since at least 1911.<sup>2,5</sup> Two of the better known anomalies are occipito-atlantal fusion<sup>4</sup>

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and failure of vertebral segmentation at the level of the second and third cervical vertebrae. Since failure of motion at a segment of the cervical spine tends to place an additional load on the next superior segment, an abnormal stress is produced at the level of the first to second cervical vertebrae. In addition to the required roentgenologic examination, the patient described in this report was also studied by cineradiography. The method of cineradiography has been reported previously.<sup>3</sup>

## Report of a Case

Six weeks before admission to the hospital, the patient, a 22-year-old white railroad switchman, fell when he jumped off a train. He rolled over repeatedly and was bruised at various places about his trunk and legs. That evening he complained of a severe cervical occipital headache, which persisted to the time of admission. It had become less severe and less frequent, however. The patient also complained of blurring of vision and some dizziness. In the hospital he complained of a feeling of "drawing up" of his legs whenever he flexed or extended the head. With these movements paresthesia was noted at times in both arms.

The patient, who was cooperative, was somewhat slender. He appeared well developed and well nourished. The neck was somewhat long and the shoulders were slender and sloping. A minimal asymmetry of reflexes was noted, with the right biceps slightly more active than the left. The right abdominal reflexes were slightly less active than the left and fatigued more rapidly, but patellar reflex was more easily elicited on the right. The plantar reflexes responded normally.

The sensory level appeared to be fairly consistent at about the fifth thoracic vertebra posteriorly and a little higher anteriorly. Position sense was definitely reduced in the toes of both feet although vibratory sensation was apparently unimpaired. Interestingly, sensitivity to pinprick over the thighs diminished considerably whenever the neck was flexed, and subjective complaints were reproduced. These changes were consistent on several examinations.

*Roentgen Studies.* Anteroposterior, lateral, and oblique projections were employed in the neutral, flexed and extended attitudes. Anteroposterior lateral laminagrams were obtained of the neck in flexion.

These studies showed incomplete segmentation

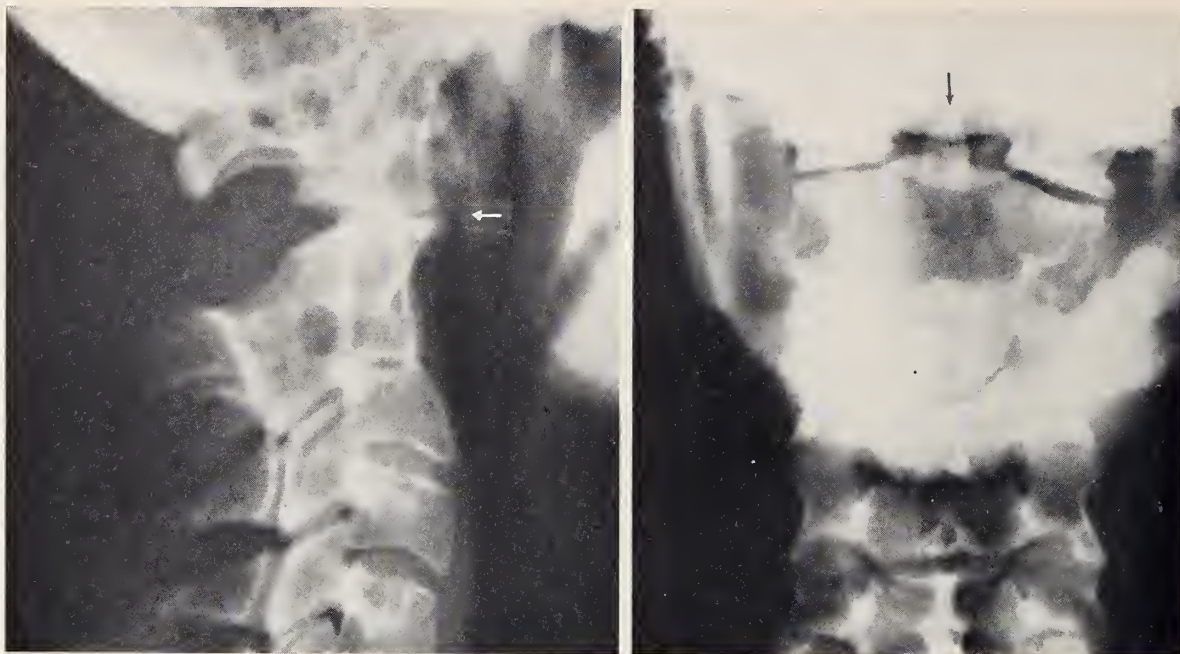


Figure 1.—*Left*, a lateral view of the cervical spine with the arrow pointing to the broad flat articulations of the first and second cervical vertebrae. This flattening is characteristic of the excessive demand produced by occipitalization of the atlas. *Right*, anteroposterior view of the cervical spine. The arrow indicates the hypoplastic odontoid process.



Figure 2.—Lateral projections of flexion and extension showing the sliding motion of the first and second cervical vertebrae. This motion is better demonstrated by cineradiography.

of the second and third cervical vertebrae and of the articular facets. The odontoid process was present but hypoplastic. The first cervical vertebra was smaller than usual in its neural arch and anterior tubercle. Extension of the odontoid process was not as far cephalad as usual, just reaching the rudimentary anterior tubercle. Roentgenograms

obtained in flexion and extension and by means of lateral and oblique projections failed to demonstrate any separation between the neural arch of the first cervical vertebra and the occiput. These views did not show difference, however, in spacing of the neural arches of the first and second cervical vertebrae. In extension, the hypoplastic odon-



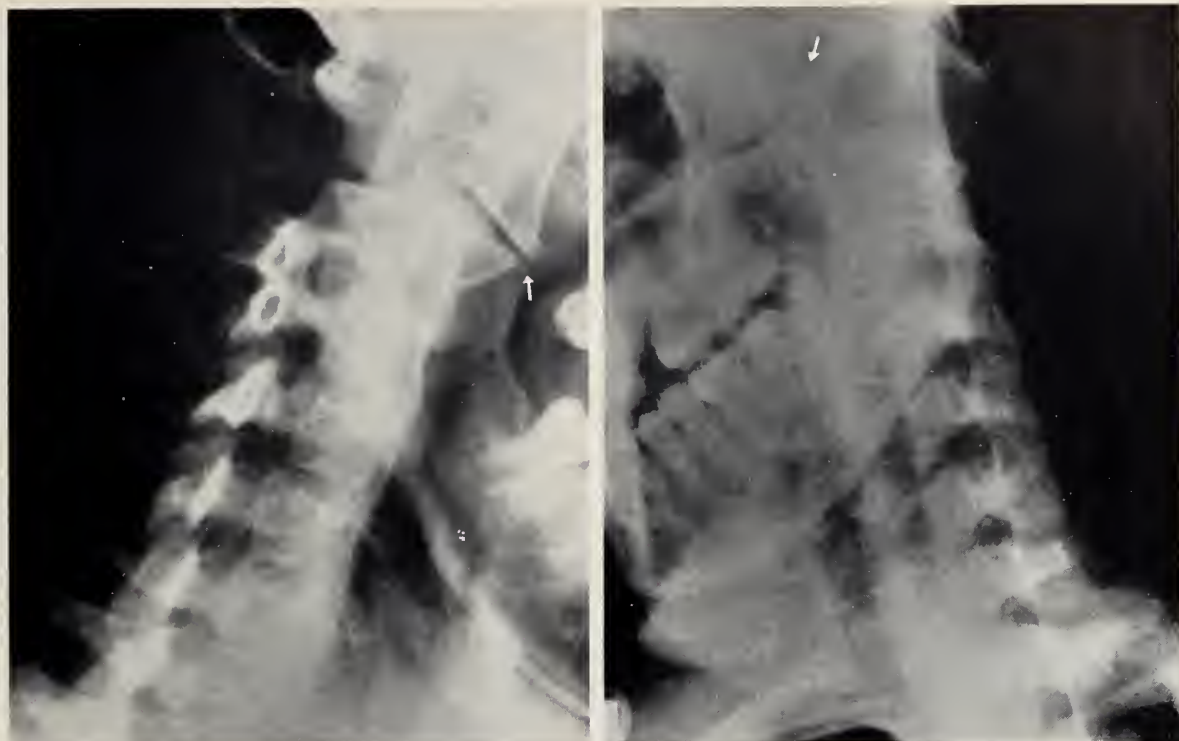


Figure 3.—Flexion in oblique projections. Film at left shows the shelf-like articular surface of the second cervical vertebra and the amount of sliding in flexion. Right, the hypoplastic odontoid is indicated by the arrow.

toid process was practically in contact with the posterior portion of the anterior tubercle of the first cervical vertebra. With flexion, however, this part of the vertebra was separated about 1 cm from the anterior aspect of the odontoid process. Not noted were fracture, coarctation of the foramen magnum or basilar invagination.

Based on the roentgenograms, the diagnosis was (a) atlanto-occipital fusion; (b) increased mobility of hypoplastic odontoid process; and (c) incomplete segmentation of the second and third cervical vertebrae.

*Cineradiographic Studies.* The motion of the cervical spine was also recorded cineradiographically. The lack of motion of the segments at the occipito-atlantal articulation and at the levels of the second to third cervical vertebrae was confirmed. The articular shoulders of the second cervical vertebra and the articulating margin of the first cervical showed developmental shaping (Figure 1). This development is consistent with the excessive demand placed upon this articulation. The atlo-axial instability could be demonstrated during otherwise imperceptible movements in its translatory phase. In extension, upward riding of the anterior arch of the atlas on the hypoplastic

odontoid process was evident. In flexion, some separation was also noted between the anterior arch of the atlas and the odontoid process (Figures 2 and 3). The rotational phase again demonstrated instability of both extension and flexion, but not of side-to-side instability.

To promote stability at the atlo-axial articulation, bone grafts were placed posteriorly, extending from the occiput to the fused second and third cervical spinous processes (Figure 4). Roentgenograms obtained a year later showed incomplete union of the bone grafts with the occiput. Bony deposit was progressive, however, along the site of the bone grafts.

## Discussion

Unless reduction in the diameter of the anteroposterior foramen is appreciable, occipitalization of the atlas may be of casual interest only.<sup>5</sup> No consistent neurologic symptoms related to fusion of the second and third cervical vertebrae have been described. With the combination of these two anomalies, symptoms are related primarily to partial fusion and instability from incomplete ligamentous attachment.<sup>1</sup> The hypoplastic odontoid process, however, has been described as a poten-



Figure 4.—Midline tomogram. The top arrow points to the very small, high-lying fused anterior arch of the atlas. The lower arrow indicates the flat articular surface of the first cervical vertebra with the hypoplastic odontoid lying well below the anterior arch of the atlas. Posterior fusion had been done before this roentgenogram was obtained.

tially dangerous lesion in that the transverse ligament may slip over the tip of the odontoid process during hyperflexion. In the patient described herein, a hypoplastic odontoid process combined with anomalies on either side of it presents a potentially severe hazard. The absence of symptoms until age 22, when a mild accident caused them to develop along with neurologic changes, is compatible with instability. When the odontoid process is absent or shows failure of union, symptoms do not usually appear until the third to fourth decade.

McRae<sup>4</sup> pointed out that pressure in the medulla oblongata is produced by the odontoid process in the flexion action with occipitalization of the atlas. The other area of pressure is from the posterior margin of the affected foramen magnum, which again results during the flexion action. In describing the normal atlanto-odontoid-basion relationship, Wholey, Bruwer and Baker<sup>6</sup> stated that the middle half of the odontoid lies directly beneath the basion. This relationship was distorted

in the present patient, as shown in Figure 4. The comments of Wholey, Bruwer and Baker regarding the asymptomatic state of patients with simple occipitalization of the atlas support the findings of other investigators. When combined with other anomalies, however, occipitalization may be clinically significant.

In the present case symptoms developed during extension, which would indicate that the instability of the first on the second cervical vertebra produces encroachment of the spinal canal. With a saddle-shaped atlas and high articulations of the atlas, the overriding of the arch of the atlas on the hypoplastic odontoid process during extension accentuates the instability. The cineradiographs enabled complete valuation of the degree of instability, particularly in the early part of extension. Hadley<sup>2</sup> reported one patient with a complex of anomalies identical to that described in the present patient, as well as congenital deformities of the feet and of the middle phalanges of all the fingers. Symptoms were related to bilateral nystagmus and diminished left ankle and left biceps reflex. Whether these were accentuated by flexion or extension of the neck was not stated.

## Summary

Neurologic changes and symptoms after minimal trauma in a 22-year-old man are described. Roentgenologic and cineradiographic studies demonstrated the lack of stability of the first cervical on the second cervical vertebra. This instability was the result of hypoplasia of the odontoid process. It was apparently accentuated by lack of mobility at the atlo-occipital joint and at the articulations of the second and third cervical vertebrae where fusion had occurred.

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# Use of Desferrioxamine In Treatment of Acute Ferrous Sulfate Intoxication

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ONE OF THE MOST distressing problems in pediatric toxicology is acute iron intoxication from ingestion of excessively large doses. The mortality rate is 25 to 50 per cent.<sup>1,2</sup> In the past two years desferrioxamine has been used in a few cases with success<sup>3</sup> and the drug appears capable of considerably reducing the mortality. The following is a case in which it was used effectively.

## Report of a Case

A 21-month-old Caucasian girl was admitted to the Woodland Park Community Hospital 16 June 1965 for treatment of acute iron intoxication due to ingestion of ferrous sulfate tablets. Earlier on the morning of admission, the patient ingested between 30 and 50 ferrous sulfate tablets, 20 mg each. She was taken to a physician's office in a pallid and lethargic state. Her hands, mouth, tongue and buccal cavity were stained with dark green material and there was profuse excretion of greenish watery stool. On gastric lavage no partially decomposed tablets were found. Fifty milliliters of Universal Antidote was instilled and oxygen was administered by mask. Procaine penicillin, 600,000 units, was given intramuscularly. Then the patient was taken to a hospital. During the trip she became more lethargic and upon admission at 11:30 a.m. she was semi-comatose. She was immediately placed in an oxygen tent.

Specimens of blood were drawn and intravenous infusion of 5 per cent dextrose in saline solution was started. Sanguinous material drained from a Levine tube placed in the stomach. Concomitantly

two green-stained stools were explosively discharged.

The blood pressure was 82/60 mm of mercury, the pulse rate 124 and respirations 24 per minute. Rectal temperature was 98.6°F. Areflexia and pronounced lethargy and pallor were noted.

A No. 8 Foley catheter was inserted into the bladder and orange-yellow stained urine was obtained. After a 100 mg test dose of edathamil, 600 mg of that drug and 20 mEq of potassium chloride were given intravenously over a three-hour period.

Hemoglobin was 16.2 gm per cent per 100 ml and the hematocrit was 48.5 per cent. Leukocytes numbered 20,500 per cu mm with differential of 70 per cent polymorphonuclear cells, 5 per cent stab forms, 24 per cent lymphocytes and 1 per cent monocytes. Blood urea nitrogen was 32 mg and creatinine 1.9 mg per 100 ml; carbon dioxide 18.6 mEq, sodium 138 mEq, chloride 108 mEq and potassium 3.1 mEq per liter. The blood pH was 7.3. Total bilirubin was 0.7 mg per 100 ml. Serum glutamic oxalopyruvic transaminase was 32 units and serum glutamic pyruvic transaminase 34 units. Total protein was 6.4 gm per 100 ml with an albumin-globulin ratio of 3.9:2.5. Alkaline phosphatase was 11.4 units. Urinalysis was within normal limits. Serum iron on admission was 510 mcg per 100 ml. The serum iron and urinary iron as determined after that are shown in Table 1.

At 5 p.m. the evening of admission, 2 gm of desferrioxamine was given through the nasal gastric tube and 500 mg was injected intramuscularly. The intramuscular dose was repeated at 12-hour intervals during the following 72 hours. Procaine penicillin was continued in doses of 600,000 units daily. The patient improved steadily. The day after admission the hemoglobin was 11.5 gm per 100 ml, leukocytes 13,900 per cu mm and the hematocrit 34.5 per cent. Serum calcium was 4.9 mEq per

TABLE 1.—Effect of Desferrioxamine in Treatment of Acute Ferrous Sulfate Intoxication—Serum Iron Content as Determined Daily, and Urine Excretion of Iron in 24-Hour Periods

Date	Serum Iron (per 100 ml)	Excreted in Urine (mg in 24 hours)
June 16, 1965.....	510 mcg	—
June 16, 1965.....	485	—
June 17, 1965.....	305	11.9
June 18, 1965.....	187	1.47
June 19, 1965.....	173	4.1
June 20, 1965.....	61	—

Note: Serum iron by Caraway method. Normal range 65 mcg to 150 mcg per 100 ml.

Submitted October 14, 1965.

liter. Electrolytes, consisting of sodium, potassium chloride and carbon dioxide, were all within normal limits. A Ham test done on the urine was negative for hemolysins.

The patient began to eat satisfactorily on the third day. She was very alert and essentially asymptomatic and she continued to make steady improvement from then on. On 21 June bone marrow aspirate was morphologically normal and contained no stainable iron. The patient was discharged in satisfactory condition the next day and remained asymptomatic thereafter.

## Discussion

Iron poisoning occurs almost entirely in children. Serum iron levels have been reported as high as 5,000 mcg per 100 ml with many in the range of 3,000 to 5,000 mcg.<sup>8</sup> However, symptoms and sequelae may occur even with serum levels of 300 mcg per 100 ml.<sup>7</sup> In the present case the course was characteristic of acute iron intoxication. About an hour following ingestion, vomiting occurs, and peripheral vascular collapse may soon follow, with tachypnea, cyanosis, pallor and neurological changes manifested by coma, areflexia and flaccidity.<sup>2</sup>

The characteristics of the gastrointestinal tract, both grossly and histologically, have been well described.<sup>2</sup> There is usually erosion and ulceration of the stomach and small intestines. In some cases (in which the patient survived) pyloric stenosis with stricture has been reported.<sup>3,4</sup> The pathogenesis is not entirely clear. It is problematical whether it is the severe necrosis of the gastrointestinal epithelium or the metabolic derangement that is responsible for the ensuing symptoms.

Desferrioxamine is a sideramine of microbial origin. It was originally developed for treatment of hemochromatosis. Its use and efficacy in acute iron intoxication is becoming well known.<sup>5,6,7</sup> The soluble hydrochloride salt binds 9.3 mg of trivalent inorganic iron per 100 mg with an avidity comparable to that of transferrin. It is not absorbed to any great extent when given orally. In the intestine

it binds inorganic iron and reduces absorption of iron. When desferrioxamine is given intravenously or intramuscularly it combines with iron to form ferrioxamine, which is excreted in the urine. To date there have been no serious side-effects reported. It has further advantage in that it appears specific for iron as opposed to other chelating agents such as EDTA, which affects other electrolytes. The rationale and efficacy of the use of desferrioxamine in acute iron intoxication is well demonstrated in this case presentation. The continuous drop in serum iron (see Table 1) with subsequent removal of iron from the bone marrow, reveals the potency of desferrioxamine's chelating ability.

## Summary

A report of a case of acute iron intoxication in which desferrioxamine was successfully used gives further evidence of the efficacy of this chelating agent in the treatment of this serum condition.

Woodland Park Community Hospital, 7011 Shoup Avenue, Canoga Park, California 91304 (Perlmutter).

ACKNOWLEDGMENT: Ciba Pharmaceutical Company made available the drug desferrioxamine (Desferal®).

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**California  
Medicine**

## EDITORIAL

### An Important New Job For CPS

THE NEW government-financed health care programs stemming from recently-enacted federal and state legislation will have the practical effect of involving California Physicians' Service-Blue Shield in payment for health care services for more than two million aged or indigent residents of California. This extension of CPS-Blue Shield activities beyond the one million persons under CPS commercial programs greatly increases the importance of the role Blue Shield plays in providing health care coverage for citizens of this state.

At the direction of the California Medical Association and with its assistance and support, CPS has successfully bid for statewide administration of the California Medical Assistance Program (the Casey Bill program), and also has been chosen to handle Part B of the Social Security Medicare Program in all California counties except Los Angeles and Orange.

The ability of CPS to fulfill its new role and successfully administer these programs will depend in large part on a cooperative effort between each of us as individual physicians, our county and state medical organizations and our fiscal arm, CPS-Blue Shield. It may also be said that the concept in the present laws establishing the physician's right to be paid a reasonable fee for his services also depends upon the results of our cooperative venture.

Achievement of the task assigned to CPS under the government programs calls for much greater reliance on local guidance than in the past. Final determination of the "reasonable charge" for a physician's services and for utilization review of these services legally rests with CPS-Blue Shield, but local professional review obviously is essential for judging both fees and utilization. County medical society review committees and Foundation review committees must assist in the establishment of general review guidelines and in the review of individual cases to assure that local practice is reflected in payment for and utilization of services. It should be clearly recognized that this involvement is not primarily to "help CPS." It is essential to the interests of the medical profession. Through the tangible results of this cooperative effort it is hoped the government may be persuaded that further direct involvement in the individual physician's practice and relationship with his patient is unnecessary and unwarranted.

Although we, as individual physicians, may not agree with the philosophy of government subsidy of medical care, we can feel considerable satisfaction that the current laws incorporate a great many concepts actively sought by the medical profession. Among these are free choice of physician and hospital, payment on a reasonable fee basis, and program administration within the medically-oriented private sector of the economy. The ability to maintain these concepts depends entirely on the degree of success achieved in the operation of the programs as they are now constituted.

Obviously a great deal of responsibility is being placed on the individual physician as well as on the organizations which represent him. Without question the new Medicare program and the Cali-

California Medical Assistance Program will, due to their magnitude, profoundly influence prepayment and health insurance concepts. The programs must prove successful in vital areas if this influence is to be in the best interest of the public and the profession.

At this time, while the government is rapidly expanding its role in the provision of medical services, it behooves us to strengthen our own Blue Shield commercial-type programs. Although the Blue Shield concept owes its existence to the medical profession in California, our own Blue Shield Plan in this state covers only a small percentage of the market in comparison with most other Blue Shield plans. At present CPS membership stands at 1,145,000 persons or about 6 per cent of the California population. Even so, through its pilot studies and program development CPS has had a significant influence on Blue Shield nationally and on the health coverage field in general.

Many have voiced the opinion that CPS should cover a much larger segment of the population, so that its influence might be greater. Others have taken the opposite view. CPS was created by physicians as a mechanism to perform social and civic service of great public benefit—to remove the financial barrier between the public and the availability of good medical care. To achieve this prepayment goal, CPS always must balance the demands of the marketplace against the demands of medical practice and the desires of the medical

community. Often it seems that the type of prepayment coverage best suited to the requirements of medical practice is not readily understood or acceptable to the purchaser of health programs. Exerting influence on accepted standards of the local market is obviously more difficult for an organization having only a minor share of the market. Only by increasing our subscriber membership can we hope to substantially influence the California general public's concept of medically sound prepayment health coverage.

The need for exerting influence on the commercial market is increased rather than diminished by the new government programs if the medical profession wishes to retain its traditional leadership in the design of health care programs, and if we hope to establish clearly in the public's mind the advantages of voluntary medically-oriented coverage.

CPS has been called upon many times during the past quarter century to undertake tasks vital to the private practice of medicine. The role is not an unfamiliar one since CPS from its very beginning has served medicine while serving the public. With the assistance and support of physicians and their societies, the Board of Trustees of CPS-Blue Shield can be confident that it will successfully meet the challenges which face us today.

WILLIAM H. THOMPSON, M.D.  
Past Chairman, Board of Trustees  
California Physicians' Service—Blue Shield

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## To All My Patients

"I did not write the medicare bill.

"I am not sure I understand it.

"I am not a government official.

"I was not trained in political economy.

"If you are not satisfied with your present, (1) medical costs or services, (2) hospital availabilities or cost, or (3) the cost of your drugs, there isn't much reason to talk it over with me—I am probably as dissatisfied as you are and probably much more confused.

"There isn't much point in discussing with me the problems you have as a result of getting a whole new system of laws (regarding your medical care) to live by, because I don't yet understand what it is all about either.

"May I humbly suggest, if you have a problem (and I sincerely hope you do not) that you write

your representative or senator in the United States Congress. Most of them knew enough about the law to vote for it, and perhaps since they knew so much about it when it was voted on, they can give you answers to all your questions now. I can't.

"Since my profession . . . is coming more and more under the control of the elected and appointed public officials in Washington, D.C., please do not expect me to become less and less a doctor. I can't. I won't. Therefore, the economic-legal-political questions that are troubling you should be taken to the experts in those fields for an appropriate answer.

"In the meantime, remember me as the one who treats your arthritis, your blood pressure, your aches and pains. The one who is concerned with your long and comfortable physical life and—I hope—your mental stability in these trying hours."

—*Reprinted from the St. Louis County (Mo.) Medical Society Bulletin.*



# California Medical Association



## NOTICES AND REPORTS

### John G. Morrison, M.D.

#### CMA President-Elect

JOHN G. MORRISON is a general practitioner in San Leandro in Alameda County. Almost everyone present is aware of his long list of accomplishments and positions in the offices of organized medicine. In preparing this nomination speech, I was awed by the variety of involvement that Jack has had in civics—medical civics and community civics. He has served on many committees of the Alameda-Contra Costa Medical Association and as its President. He was a Councilor of the California Medical Association for four years; for six years he was on the Board of Trustees of the California Physicians' Service, and for half of that time was chairman. For five years he has ably represented the CMA in its delegation to the American Medical Association. These posts are merely representative; there are many more in which he has served medicine well.

What many may not know is Dr. Morrison's involvement in areas outside of organized medicine. He has been on his local Selective Service Board for 18 years; he is consultant to the Bureau of Medicine of the Federal Food and Drug Administration in Washington; he represents medicine on the Task Force on Institutional Care of the California Health and Welfare Agency. He is a member of the Governor's Conference on Aging, a consultant to the Bay Area Health Facilities Planning Commission, a leader in his local hospi-



JOHN G. MORRISON, M.D.

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tal staffs. His experience in the complexities of medical problems has prepared him outstandingly for the responsibilities of President-Elect of the California Medical Association.

This is only a partial recitation of Dr. Morrison's responsibilities and accomplishments, and of the equipment in experience and qualities that he will bring to this job. Some other assets include the famous happy Morrison smile, his ability to maintain his equanimity under the most trying and irritating of circumstances, his ability to extract effort, advice, help and cooperation from those around him, and to choose those people well. Some of his other assets are Mary Lou Morrison, his lovely and vivacious wife, who is active in the local and state Woman's Auxiliary, and six stalwart sons who have been distributed to medical

school, the army, the business world, engineering, and high schools.

Beyond this biographical recitation with which we put Dr. Morrison's name into nomination as President-Elect, the Alameda-Contra Costa delegation wants to share with you the deeper feelings of admiration and respect it holds for Jack as a friend, father, citizen and physician. We are most pleased to be able to honor him with nomination to this high office in the largest state medical society in the country, and I hope I can convey to you even a little of the warmth of our feelings for this truly sensitive, friendly, wonderful guy who has earned and holds so big a place in the hearts of all of us.

J. BRANDON BASSETT, M.D.  
*President, Alameda-Contra Costa  
Medical Association*





## Council Meeting Minutes

*Tentative Draft: Minutes of the 518th Meeting of the Council, Hyatt House, San Francisco, 19 February 1966.*

The meeting was called to order by Chairman Anderson in the Hyatt House, San Francisco, Saturday, 19 February 1966 at 9:40 a.m.

### *Roll Call*

Present were President Teall, President-elect MacLaggan, Speaker Quinn, Vice-Speaker Telford, Editor Dwight L. Wilbur, Secretary Hosmer and Councilors Isenhour, Melone, Todd, Bullock, O'Connor, Rogers, Burnett, Richard S. Wilbur, Miller, Watts, Fenlon, Kay, Kaiser, Taw, Anderson, Yant, Grunigen and Shaw. Absent for cause were Councilors Wilson, Gooel, Ham and Maguire and Immediate Past President Doyle.

A quorum present and acting.

Present by invitation were Messrs. Clancy, Collins, Klutch, Eberlein, Thomas, Goldman, Clark, Moreillon, Garrick, Edwards, Doctor Miller, Mrs. Griffith, Miss Price and Mrs. Redfern of CMA staff; Messrs. Hassard and Huber, legal counsel; component society executives Scheuber of Alameda-Contra Costa, Geisert of Kern, Sommerville of Napa, Bannister of Orange, Dochtermann of Sacramento, Donmyer of San Bernardino, Neick of San Francisco, Wood of San Mateo, Marvin of Santa Barbara, Brown of Sonoma, Bruce of Tulare, Pearce of Santa Clara, Monnich of San Joaquin, Rosenthal of Los Angeles and Jackson of San Diego; Doctor Lester Breslow, director of the Department of Public Health; Doctor William Thompson and Messrs. Saylor, Wahlberg, Potloff and Babb of California Physicians' Service; Messrs. Read, Salisbury, Putnam and Brown of the Public Health League; Mr. Jerry Gould of the AMA; Mr. Richard Layton of AMPAC; Mr. Henry X. Jackson, president-elect of the California Hospital Association; Doctors Bostick, Boyers, Herzog, Cook, Kilroy and others.

### *1. Recognition of Doctor Ivan C. Heron*

Chairman Anderson announced the death of Doctor Ivan Heron, long-time leader of the CMA.

He served for many years as Vice-Speaker of the House of Delegates. This 518th meeting of the Council was dedicated to his memory.

### *2. Minutes for Approval*

Minutes of the 517th meeting of the Council, held 16 January 1966, were approved, with three corrections. These corrections were:

(a) Notation of correct address for Doctor Milton Van Riesen. It should be Glendale instead of Palo Alto, as listed in the report of the Committee on Committees.

(b) Under Item 11, Mr. Henry X. Jackson is president-elect of the California Hospital Association, not Mr. Charles Jackson.

(c) Addition of a commendatory resolution on AMA-ERF to be submitted to the House of Delegates. The Resolved portion reads:

**RESOLVED:** *That the California Medical Association reaffirm its positive support of AMA-ERF and the projects it sponsors by developing state and local AMA-ERF committees to assist the Board of Directors and the staff of AMA-ERF in their efforts to increase physician understanding and voluntary financial support for AMA-ERF projects.*

### *3. Membership*

(a) On motion duly made and seconded, one member whose dues were delinquent and now paid, was reinstated.

(b) On motion duly made and seconded, 26 applicants were voted election to Associate Membership. These were:

Wm. J. Cassel, Jr., Alameda-Contra Costa County; Frederick M. Hebert, Leon Edgar Wesner, Fresno County; Abraham T. K. Cockett, G. C. Emmanouiledes, Wm. M. Fowler, Jr., Gertrude Fox, David B. Friedman, Bernard H. Gale, Warren Harris, John G. Mohler, James Roger Nelson, Robert S. Rosen, Julius R. Scholtz, Lee Shropshire, Robert L. Wick, Jr., Los Angeles County; Harold G. Burden, Napa County; Martha C. Wager, San Diego County; Samuel B. Aronson, Aileen Grant, San Francisco County; Charles M. Colianni, Daniel Krag, William Sproul, Santa Clara County; Alfred C. Hanscom, Santa Cruz County; Lida C. Brown, Tulare County; Gerald K. Ridge, Ventura County.

(c) On motion duly made and seconded, 20 members were voted election to Retired Membership. These were:

Philip J. Dick, John Ohanneson, Alameda-Contra Costa County; Allan R. Watson, Hum-

boldt-Del Norte County; Maurice N. Beigelman, Herschel S. Burns, Rufus Alonzo Davis, Carl Erich Ebert, Carl F. Grunewald, Lillian Kositz, Fred S. Lindheimer, Robert F. McBratney, Joseph L. Robinson, Los Angeles County; Michael F. DeSalvo, San Bernardino County; Melvin H. Knoepp, Thomas M. McMillan, San Diego County; Hazel Nicola Woodruff, Solano County; Gerald E. Davis, San Mateo County; Pearl V. Konttas, Donovan C. Oakleaf, Sonoma County; Fred G. DeBusk, Tulare County.

(d) On motion duly made and seconded, a reduction of dues was voted for 34 members for reasons of prolonged illness or postgraduate education.

#### 4. Report of the President

President Teall reported on his visits to county societies and districts, a meeting with the Workmen's Compensation Industry Medical Committee, a public hearing on implementation of Assembly Bill 5 before the Assembly Committee on Social Welfare, a statewide conference on rural health and safety, a regional meeting of the Health Insurance Council in Phoenix, and others.

#### 5. Workmen's Compensation

Doctor Anderson presented an interim report on implementation of Assembly Bill 2023, which involved changes in the workmen's compensation system. He noted that the "Register" questionnaire material recently mailed to physicians does not bind any party to participation or to level of fees. The questionnaire is to be used for informational purposes only—in achieving wider choice of physicians for care of occupationally injured persons.

**ACTION:** Voted to send to CMA delegates, alternates and others a clarifying letter on the intent of the CMA in circulating a questionnaire on a "Physician Register" to be used in the Workmen's Compensation System.

#### 6. Component Society Officers Conference

Doctor L. Morgan Boyers, 1966 conference chairman, presented a detailed report of reactions to the 1966 meeting and a series of recommendations for future conferences. The primary recommendation concerned more involvement of physician leaders and executive secretaries at the local level in planning the conferences.

**ACTION:** Voted to accept the report of the 1966 Conference Planning Committee and to thank the group for an excellent meeting this year.

#### 7. California Medicine

Editor Dwight L. Wilbur called attention to an "outdated" provision in the CMA Constitution and Bylaws which requires that any paper presented at the Annual Session becomes the property of the California Medical Association and that the author cannot cause it to be published elsewhere than in CALIFORNIA MEDICINE except with the consent of the Editorial Board. Doctor Wilbur proposed an amendment to the Constitution and Bylaws which would eliminate this requirement.

**ACTION:** Voted to submit a resolution to the House of Delegates altering the language regarding submission of papers to California Medicine.

#### 8. Health Review and Program Council

Councilor Miller reviewed some recent recommendations and activities of the Health Review and Program Council, a body established under Assembly Bill 5. It is now serving in an ad hoc capacity until the Council can be officially activated after 1 March 1966. He emphasized that some informed sources believe that either the scope of benefits or the eligibility rules will need revision for the "medically indigent" under A.B. 5, since the potential recipient load is so large.

#### 9. Committee on Committees

Doctor MacLaggan presented a list of recommendations for appointment to commissions and committees. These recommendations will come before the Council officially at its meeting in March and then be submitted to the House of Delegates.

The Committee on Committees also recommended:

(a) That the Committee on Veterans Affairs be made a standing committee.

**ACTION:** Voted to recommend to the House of Delegates that the Committee on Veterans Affairs be a standing committee.

(b) That the name of the Bureau of Research and Planning be changed to the Bureau of Research and that its activities and working relationships with commissions and committees continue on its present basis.

(c) That the Committee to Study the Role of Medicine in Society be made a committee of the Council. This committee would continue to be responsible for long-range planning and examination of external factors concerning medicine.



(d) That a new committee of the Council be created to be called the Committee on Organizational Review and Planning. This new committee would be charged with the responsibility for short-range planning and the continuing review of organizational activities.

**ACTION:** *Voted that the name of the Bureau of Research and Planning be changed to the Bureau of Research and that its activities be restricted to research.*

**ACTION:** *Voted that the Committee to Study the Role of Medicine in Society be separated from the Bureau of Research and Planning but remain as a committee of the Council.*

**ACTION:** *Voted that the CMA create a Committee on Organizational Review and Planning as a standing committee of the Council.*

(e) That Doctor Richard H. Schugg of Long Beach be added to the State Department of Education advisory committee for medical assistants' courses.

**ACTION:** *Voted to approve the recommendation.*

(f) That Doctor Gerald Hill of San Rafael be designated as a second CMA representative on the California Interagency Council on Cigarette Smoking and Health.

**ACTION:** *Voted to approve the recommendation.*

(g) That Doctor David Rubin of Los Angeles be designated as a representative to assist in the planning of the Fourth National Biomedical Sciences Instrumentation Symposium.

**ACTION:** *Voted to approve the recommendation.*

(h) That the three physician representatives on the California Committee on Fitness of the State Department of Education, whose terms are expiring, be continued as CMA representatives. They are: Doctors Donald Fowell, Stockton; Homer Graham, Burbank; and Hartzell Ray, San Mateo.

**ACTION:** *Voted to approve the recommendation.*

(i) That the Council direct the Committee on Welfare Medical Care Programs to study the impact of the Economic Opportunity Act and other anti-poverty legislation and their relationship to the provision of medical care in economically impoverished areas.

**ACTION:** *Voted to approve the recommendation.*

#### 10. *Affiliated Organizations and Invited Guests*

Representatives of several organizations, medical schools and departments of state government

reported on activities of interest to the Council and the medical profession. No action was required. Among those present were Doctor Lester Breslow, director of the Department of Public Health; Doctor Warren Bostick, dean of the UC-California College of Medicine; Doctor Charles J. Tupper, newly-appointed dean of the UC School of Medicine at Davis; Dr. Fernando Torgerson, director of the Office of Health and Medical Care Services, Health and Welfare Agency; Mr. Henry X. Jackson, president-elect of the California Hospital Association; Doctor Robert J. Glaser, dean of the Stanford School of Medicine.

#### 11. *Certification of Non-Accredited Hospitals*

Doctor Bert Halter, chairman of the Commission on Hospital Affairs, and others have met with representatives of the Department of Public Health regarding the feasibility of having CMA medical staff survey teams inspect non-accredited hospitals (medical staffs) in California for possible certification under Public Law 89-97.

**ACTION:** *Voted to authorize the Committee for Emergency Action to enter into contractual arrangements with the Department of Public Health for medical staff inspections of non-accredited hospitals, if the terms seem appropriate.*

#### 12. *California Physicians' Service (Blue Shield)*

Doctor William Thompson, board chairman, introduced Mr. R. S. Saylor, acting president of CPS; announced a membership gain last year of 30,000; discussed contract negotiations with the State on Assembly Bill 5; announced plans of communications with physicians on billing procedures and other specifics under the "fiscal intermediary" arrangement for A.B. 5; informed the Council of developing plans to serve as a carrier under Part B, Title XVIII, P.L. 89-97.

#### 13. *1968 Annual Session of the California Medical Association*

Inasmuch as the year 1968 will be the centennial year of the oldest medical society in California (The Sacramento Society for Medical Improvement), Doctor Orrin Cook, current president, issued a formal invitation for the CMA to hold its annual meeting in Sacramento that year. No action was taken, pending investigation of possible arrangements by staff.

#### 14. *Finance Committee*

Doctor Harold Kay, chairman of the Finance Committee, presented a final report and series of

recommendations regarding the budget for fiscal year 1966-67.

The Finance Committee recommended:

(a) That the current \$10 per member donation to AMA-ERF be reduced to \$5 per member.

(b) That a constitutional amendment be introduced in the House of Delegates to the effect that the \$1 per member contributed to the Physicians' Benevolence Fund be eliminated as a compulsory allocation, and that authority to allocate funds rest with the Council.

(c) That the dues be raised from \$75 to \$90 per member beginning 1 January 1967.

(d) That the proposed budget, including provision for expansion of activities, be accepted by the Council for recommendation to the House of Delegates.

Councilor Bullock proposed an addition of approximately \$5,000 to the budget for use of medical libraries, this being an amendment to the motion on the budget.

**ACTION:** *Voted to insert the same amount of monies specified in the 1965-66 budget (\$5,000) in the CMA budget for the LACMA Library.*

**ACTION:** *Voted to accept the recommendations, as amended, of the Finance Committee (which must be submitted to the House of Delegates) that the proposed budget be approved; that AMA-ERF contributions be reduced from \$10 to \$5 per member, that the \$1 per member contribution to the Physicians' Benevolence Fund be eliminated; and that dues be set at \$90 per member beginning 1 January 1967.*

#### 15. Student American Medical Association

The 1966 annual meeting of the Student American Medical Association has been scheduled for Los Angeles. SAMA requested a \$500 contribution to help finance part of the program.

**ACTION:** *Voted to contribute \$500 to the Student American Medical Association to defray some of the expenses connected with its 1966 meeting.*

#### 16. Alcoholism Control Program

The CMA Committee on Public Health called the attention of the Council to Senate Bill 1279, enacted by the 1965 California Legislature, which contained a provision for "a termination date of the Alcoholic Prevention, Treatment, Control and Rehabilitation Program administered by the Department of Public Health." The CMA has been urged to support a joint legislative resolution which will clarify the intent of the termination date to mean an administrative review of the program, but *not* a cut off of it.

**ACTION:** *Voted to support a joint legislative resolution clarifying the intent of the termination date under Senate Bill 1279, to mean an administrative review of the program, but not a cut off of it.*

#### 17. Commission on Community Health Services

Chairman Harold Kay presented a series of recommendations from the Commission.

Resolution 2-65 called for the installation of a yellow caution light on the rear of automobiles which will illuminate when the throttle is in the idle position, and go off when the brake is applied and the red stop light activated. The Commission recommended that the resolution be dropped.

**ACTION:** *Voted to accept the recommendation of the Commission.*

The Committee on Automotive and Traffic Safety has developed a driver education tape on the attitudes and aptitudes of teenage drivers, the tape to be distributed to public schools and other organizations.

**ACTION:** *Voted to accept the Driver Education Tape as proposed.*

U.S. Senate Bill 2184 (co-authored by Senator George Murphy of California) proposes that certain regulations be established to control clinical laboratories dealing in interstate commerce. Senator Murphy asked for medical advice on the intent and language of the proposed bill.

**ACTION:** *Voted to take no official position on the legislation, but to offer to Senator Murphy for his advice the letters and documents submitted by pathologists and others.*

#### 18. Scientific Board

An ad hoc Committee of the Scientific Board presented a report endorsing and supporting the concept of regional dialysis centers as described in Assembly Bill 2202.

**ACTION:** *Voted to approve the establishment of two regional dialysis centers in California by the granting of state funds to existing institutions (although the CMA opposes construction of new, i.e., independent, facilities) for the operation of these centers, with the understanding that funding procedures be similar to those currently under the Hill-Burton-Harris hospital construction program.*

#### 19. Committee on Other Professions

A proposal to publish a "Joint Statement on the Role of the Nurse in Drawing Blood for Test Purposes" (CMA and the California Nurses' Association as sponsors) was presented by Doctor Forest Grunigen.



**ACTION:** *Voted to approve an amended draft of the statement which reads: "The Medical Practice Act, in general, reserves to licensed physicians the right to penetrate the skin in the health care of persons. The California Medical Association recognizes the propriety of a registered nurse properly trained in intravenous technique to draw blood samples for test purposes, if done under the order of a licensed physician."*

#### *Adjournment*

There being no further business to come before it, the meeting was adjourned at 4:15 p.m. in memory of Ivan C. Heron, M.D.

CARL E. ANDERSON, M.D., *Chairman*

MATTHEW N. HOSMER, M.D., *Secretary*

## **Occupational Health**

### **Medical Supervision of Organic Phosphate Pesticide Workers**

*A Statement of the California Medical Association prepared by the Committee on Occupational Health*

THE MEDICAL SUPERVISION of employees potentially exposed to toxic materials requires the mutual understanding and cooperation of employer and responsible physician.

1. Physicians who undertake responsibility for medical supervision of employees where organic phosphate injurious materials (organic phosphate pesticides) are handled do so with the following understanding:

- a. That the employer will have specifically engaged their services to give medical supervision.
- b. That each employee to be supervised is sent to the physician's office before exposure and as often as required by the doctor; and that medical services and laboratory tests which the physician considers essential to such medical supervision shall be authorized by the employer and required of the employee.

c. That each supervised employee is empowered by his employer to contact or visit the responsible physician whenever he:

1. has a known overexposure to an organic phosphate pesticide.
2. feels symptoms suggestive of poisoning by such pesticides.

d. That the physician (and the approved clinical laboratory\* he selects) shall be notified in writing whenever a supervised employee terminates his assignment to work with organic phosphate injurious materials.

2. Medical supervision requires pre-exposure tests to determine the blood level of both red cell and plasma cholinesterase. The physician will order these original tests performed and will then establish the schedule of rechecks based upon the worker's exposure and experience and upon the physician's judgment of need.

*Example:* New inexperienced workers may need several tests or rechecks at weekly intervals to insure that work practices are not affecting health. Experienced workers may be much less closely checked—up to eight-week intervals, if exposure is minimal. ("Tests" mean blood cholinesterase level of red cells and plasma. "Check" and "Re-check" may mean medical examination, tests, or both tests and medical examination.)

3. Responsibilities of the physician:

- a. The physician should, at the initial employee visit, obtain identifying, occupational, and medical information pertinent to protecting the employee working in organic phosphate exposure. He should also advise the employee regarding personal protection. Such medical education of the employee is not, however, a substitute for on-the-job training in safe practices, which is the employers' responsibility.
- b. The physician should confirm, in writing, verbal instructions given to employee or employer.
- c. The physician should endeavor to be conversant with the work practices and exposures of those he supervises medically.
- d. The physician should be conversant with emergency treatment of organic phosphate poisoning and will maintain or arrange for

\*A list of such approved laboratories is available from the Division of Laboratories of the State Department of Public Health, Berkeley 94704.

- adequate supplies of medication to be available for use under his direct supervision.
- e. The supervising physician should provide the employer with written instructions for emergency procedures in the event of over-exposure to organic phosphate pesticides.
  - f. The supervising physician takes responsibility for arranging adequate care for occupationally injured employees, but does not necessarily include providing medical treatment himself. He reserves the right to refer occupationally injured employees for hospitalization, consultation, or other medical care as needed.
4. The following are considered good medical practice:
- a. Cholinesterase testing:
    1. Ordered as a baseline, at a time when the worker has not been exposed to any of the organic phosphate pesticides for at least a month.  
(Caution: Certain carbamate pesticides will also lower cholinesterase levels, but for less than 24 hours.)
    2. Repeated at regular intervals while employees are regularly working with the toxic "phosphates" such as parathion, Thimet, demeton (Systox), phosdrin, methyl parathion, TEPP, EPN, OMPA, Disyston, and Bidrin.
    3. Repeated at any time a worker becomes sick while working with, or within 12 hours of his last exposure to, a toxic "phosphate" pesticide.
    4. If a worker dies within 24 hours of his last exposure to a toxic organic phosphate pesticide, a cholinesterase test should be performed postmortem.
  - b. Interpretation of routine tests for those regularly working with the organic phosphate pesticides.
    1. *Satisfactory*: When both plasma and red cell cholinesterase activity are 75 per cent or more of the individual's baseline value.
    2. *Caution—Showing significant exposure*: When *either* plasma or red cell cholinesterase activity drops to 50 to 74 per cent of the baseline value.
    3. *Stop work with organic phosphate pesticides*: When either plasma or red cell cholinesterase activity drops below 50 per cent.
    4. *Back to usual work*: When *both* plasma and red cell cholinesterase activity have risen to 75 per cent, or above the individual's baseline value.  
  
(Note: Symptoms and/or signs suggestive of organic phosphate poisoning demand continuous close medical observation, meticulous decontamination, and treatment for at least 24 hours, or until symptom free four hours after last medication.)
  - c. Where doubt exists regarding interpretation of the cholinesterase level, consult *Clinical Handbook on Economic Poisons—Emergency Information for Treating Poisoning—Wayland J. Hayes, Jr., M.D., Ph.D., Public Health Service Publication #476 Revised 1963. Obtainable from The Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C. Price 55 cents.*
- Note:* We wish to acknowledge the fine initial work done by the Occupational Health Committee of the Santa Cruz Medical Society, and the later modifications of their work recommended by the Industrial Health Committee of the Alameda-Contra Costa Medical Association, from which this statement was largely formulated. Samples of certain model forms for referral, etc. are available from the California Medical Association.



*16th annual  
regional  
postgraduate  
institute*

*AHWAHNEE HOTEL*

*Yosemite*

*May 13-14, 1966*

**SAN JOAQUIN VALLEY COUNTIES**

Presented cooperatively by San Joaquin Valley Counties Medical Societies, Continuing Education in Medicine and Health Sciences, University of California School of Medicine, Los Angeles, and the Committee on Continuing Medical Education, California Medical Association.

**HOST:** Fresno County Medical Society  
*Regional Chairman:* Dale Kirkegaard, M.D.,  
2432 Calaveras Street, Fresno.

**INSTITUTE FEE:** \$15:00. For additional information contact Continuing Medical Education office, California Medical Association, 693 Sutter Street, San Francisco 94102. All California Medical Association members and their families are cordially invited to attend.

**GUEST SPEAKER:** Michael E. DeBakey, M.D., Professor of Surgery and Chairman, Cora-Webb Mading Department of Surgery, Baylor University College of Medicine, Houston.

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**PROGRAM THEMES:**

**HEADACHE . . . CEREBRAL AND OTHER  
VASCULAR DISEASES**

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**FRIDAY, MAY 13**

*Morning Session*

- 9:00—**Diagnosis and Selection of Cases for Major Arterial Reconstruction**—Wiley F. Barker, M.D.
- 9:55—**Conservative Management of Occlusive Disease**—Peter G. Gaal, M.D.
- 11:00—**Renovascular Hypertension**—Joseph J. Kaufman, M.D.
- 11:50—**CONCURRENT WORKSHOPS** (you may go to one of your choice):
- A. **Complications of Vascular Reconstruction**—Wiley F. Barker, M.D., Moderator, Peter G. Gaal, M.D., and Joseph J. Kaufman, M.D.
  - B. **Neurological Complications of Cervical Arthritis**—Theodore L. Munsat, M.D., Moderator, Robert N. Baker, M.D., and Ulrich Batzdorf, M.D.

*Afternoon Session*

- 2:30—**Differential Diagnosis of Headache**—James R. Nelson, M.D.
- 3:15—**Migraine**—Theodore L. Munsat, M.D.

- 4:15—**The Dizzy Patient**—Augustus S. Rose, M.D., Moderator, James R. Nelson, M.D., and Morton K. Rubinstein, M.D.

**SATURDAY, MAY 14**

*Morning Session*

- 9:00—**Headache Due to Metabolic Disease**—Morton K. Rubinstein, M.D.
- 9:30—**Headache Due to Intracranial Disease**—Ulrich Batzdorf, M.D.
- 10:00—**Headache—Panel Discussion**—Ulrich Batzdorf, M.D., Theodore L. Munsat, M.D., James R. Nelson, M.D., Morton K. Rubinstein, M.D.
- 10:45—**Aortic Aneurysms**—Michael E. DeBakey, M.D.
- 11:30—**Aneurysms**—Wiley F. Barker, M.D., Moderator, Michael E. DeBakey, M.D., and Peter G. Gaal, M.D.

*Afternoon Session*

- 2:00—**Occlusive Disease of Extraeranian Cerebrovascular Tree**—Michael E. DeBakey, M.D.
- 2:45—**Occlusive Disease of the Extracranial Cerebrovascular Tree from the Point of View of the Internist**—Robert N. Baker, M.D.

### Evaluating Postgraduate Courses

PHIL R. MANNING, M.D.

*Associate Dean, Postgraduate Division, University  
of Southern California School of Medicine,  
Los Angeles*

EACH YEAR throughout the United States thousands of physicians attend hundreds of postgraduate medical programs. In the current year the medical schools of the United States will offer 1,513 courses amounting to more than 36,000 hours of instruction. Stated another way, the hours of instruction available to the American physician in the next 12 months would, if taken serially, require more than four years to complete.

In California alone six medical schools will offer 6,432 hours of instruction. To these figures must be added the thousands of hours that are spent in educational meetings at the hospital staff level as well as the many other organizations that are offering programs for the practicing physician. It is quite clear that whatever else one can say about postgraduate medical education, no one can deny the tremendous amount of time and energy that is being expended on it. Yet, there is no evidence that existing postgraduate programs are helping the practicing physician to the greatest degree possible to take better care of his patients. There is no evidence that the time devoted to postgraduate medical education is being spent most efficiently and most effectively.

In addition, there is no evidence that the medical schools and other organizations in the field are presenting material that physicians need to know for the practice of good medicine. There is the usual running discourse among medical school faculties and practicing physicians about the material that should be presented. Generally speaking, physicians in practice are most interested in learning things that they can use. Medical school faculties are accused of being most interested in presenting material on research that may not have immediate application to the practicing physician or material on obscure clinical situations which has limited applicability outside of a research institution.

It is said that approximately 70 per cent of the practicing physicians in the state of California never attend postgraduate programs. The reasons must be varied; yet one reason that a majority of physicians do not attend courses must be that they feel that the courses would not benefit them in caring for their patients.

It is time that the physicians of California lead the way in a cooperative study which will develop knowledge to determine the value of postgraduate courses with an eye to improving the learning experiences available to the practicing physicians. Several questions would be in order: (1) How valuable are the traditional postgraduate programs? (2) What subjects are most important or most beneficial for the practicing physician to learn in terms of patient care? (3) What teaching methods are most valuable in postgraduate situations? Working together, the CMA and medical schools should be able to find answers to these questions. To do this would require cooperation from the practicing physicians in the state. It might be necessary for the practicing physicians to participate by taking part in written examinations, interviews and, perhaps, even allowing members of the medical school faculties to visit their offices to learn first hand the problems that the physicians must face.

One can imagine that if every postgraduate program that was sponsored by a medical school were preceded and followed by a written examination, the value of the current postgraduate programs, as devices for the transfer of information, would be better understood. Unfortunately, most of us have negative feelings toward taking examinations, as they remind us of stressful situations that we experienced in high school, college, medical school and various board examinations. Most of us associate examinations with punitive measures which the faculty may thrust upon defenseless students. Nevertheless, the examination can be valuable in assessing the worth of teaching sessions. Indeed the experience need not be stressful but, if used correctly, can be rewarding to both the physician and faculty. In addition to purely evaluative functions, testing before and after the course should be an excellent teaching aid which could in itself improve postgraduate courses.



Perhaps such testing would help us, first of all, to know whether our current approach is of value; almost surely we would learn that some methods of instruction are better than others. As teaching aids, the testing before and after the courses would benefit the teaching situation by focusing the attention of the faculty on the fact that facilitation of learning and not presentation of facts is the main function of the instructor. Testing of this kind would also influence the faculty's determination of what is the most important material to be taught. Perhaps it would require the faculty to be more specific in its teaching. The testing might also help the student physicians focus their attention on the most important material, and it could help the learner assume a more active role in the learning process than is generally provided in the average postgraduate program. Finally, the testing might serve as a memory aid in recalling important information.

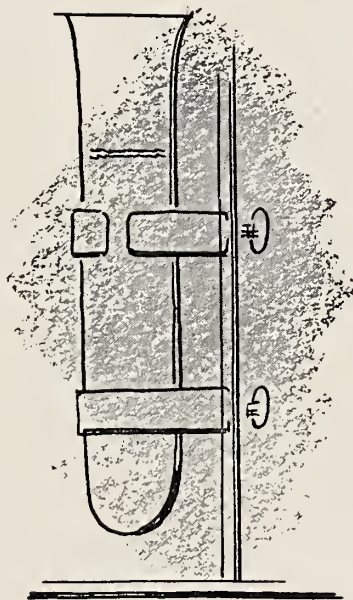
Above all, the proper use of testing before and after courses could lead to a reappraisal of our current postgraduate activities and stimulate our

energies to improve the types of postgraduate experiences that could be made available to the practicing physician.

For purposes of evaluating postgraduate courses, it would not be necessary to identify the participating physicians by name. It would be only necessary that they be identified by numbers so that their scores on tests before the course could be compared with those on tests after the course.

Concurrently with evaluating methods of presentation, it is extremely important that the medical schools and the physicians of the California Medical Association join forces to help appraise what subject material can be most beneficial to the practicing physician in his quest for what will enable him to give the most effective care to his patient.

The evaluation of postgraduate medical education will require considerable time and energy, some money and, above all, cooperation. However, the fruits of such labor should be rewarding to the practicing physician, to medical school faculties and, most important, to the patient.



## In Memoriam

BENNETT, CHARLES ROSS, Merced. Died 12 February 1966, in Merced, aged 50, of heart disease. Graduate of the University of Louisville School of Medicine, Kentucky, 1939. Licensed in California in 1949. Doctor Bennett was a member of the Merced County Medical Society.



BRESLIN, FRANK J., Los Angeles. Died 1 March 1966, in Los Angeles, aged 71, of heart disease. Graduate of the College of Physicians and Surgeons, Medical Department, University of Southern California, Los Angeles, 1917. Licensed in California in 1917. Doctor Breslin was a member of the Los Angeles County Medical Association.



BUTTRAM, C. A., Mendota. Died 20 November 1965, aged 65, of myocardial infarction, coronary artery thrombosis, and coronary atherosclerosis. Graduate of the University of Oklahoma School of Medicine, Oklahoma City, 1938. Licensed in California in 1945. Doctor Buttram was a member of the Fresno County Medical Society.



CLAUSEN, EDWIN G., Berkeley. Died 12 February 1966, in Piedmont, aged 55, of carcinoma of the stomach. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1936. Licensed in California in 1936. Doctor Clausen was a member of the Alameda-Contra Costa Medical Association.



DAVISON, CLAUDE LORRAINE, Los Angeles. Died 10 February 1966, in Los Angeles, aged 65, of carcinoma of the lungs. Graduate of the University of Illinois College of Medicine, Chicago, 1926. Licensed in California in 1927. Doctor Davison was a member of the Los Angeles County Medical Association.



DE RUSHA, DONALD WILLIAM, COSTA MESA. Died 26 February 1966, in Costa Mesa, aged 37, of coronary artery disease. Graduate of Northwestern University Medical School, Chicago, Illinois, 1955. Licensed in California in 1956. Doctor De Rusha was a member of the Orange County Medical Association.



DE VALINGER, HENRY C., Gardena. Died 10 December 1965, aged 40, of cancer. Graduate of Jefferson Medical College of Philadelphia, Pennsylvania, 1950. Licensed in California in 1958. Doctor de Valinger was a member of the Los Angeles County Medical Association.



DOZIER, ELIZABETH GIST, San Fernando. Died 26 February 1966, aged 76. Graduate of the University of Illinois College of Medicine, Chicago, 1928. Licensed in

California in 1928. Doctor Dozier was a member of the Los Angeles County Medical Association.



FAIRES, LUCIUS BENJAMIN, Hollywood. Died 15 February 1966, in Los Angeles, aged 72, of gram-negative septicemia. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1925. Licensed in California in 1925. M.D. degree from California College of Medicine, 1962. Doctor Faires was a member of the Los Angeles County Medical Association.



FORD, ROSCOE AARON, Los Angeles. Died 1 December 1965, in Los Angeles, aged 71, of coronary artery disease. Graduate of Northwestern University Medical School, Chicago, Illinois, 1921. Licensed in California in 1923. Doctor Ford was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



FRY, FREDERICK XAVIER, JR., Monterey. Died 1 February 1966, in Monterey, aged 42, of heart disease. Graduate of Creighton University School of Medicine, Omaha, Nebraska, 1951. Licensed in California in 1952. Doctor Fry was a member of the Monterey County Medical Society.



FULMER, CHARLES C., San Francisco. Died 2 March 1966, in San Francisco, aged 71, of heart disease. Graduate of the College of Physicians and Surgeons, Los Angeles, 1921. Licensed in California in 1921. Doctor Fulmer was a member of the San Francisco Medical Society.



GARNER, GEORGE WILLIAM, Carmel Valley. Died 6 February 1966, in San Francisco, aged 66, of heart disease. Graduate of Northwestern University Medical School, Chicago, Illinois, 1925. Licensed in California in 1925. Doctor Garner was a member of the Kern County Medical Society.



HASS, CLARENCE EARL, Berkeley. Died 1 March 1966, in Berkeley, aged 60, of bronchopneumonia. Graduate of the State University of Iowa College of Medicine, Iowa City, 1934. Licensed in California in 1936. Doctor Hass was a member of the Alameda-Contra Costa Medical Association.



JOHNSON, DONOVAN, Santa Ana. Died 11 February, 1966, aged 66. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1924. Licensed in California in 1924. Doctor Johnson was a member of the Orange County Medical Association.



KAVEN, HENRY A., Oakland. Died 8 March 1966, in Oakland, aged 53. Graduate of the University of Illinois College of Medicine, Chicago, 1937. Licensed in California in 1940. Doctor Kaven was a member of the Alameda-Contra Costa Medical Association.



KELLY, FRANK JOSEPH, Tiburon. Died 5 February 1966, in Tiburon, aged 42. Graduate of Washington University School of Medicine, St. Louis, Missouri, 1945. Licensed in California in 1955. Doctor Kelly was a member of the San Francisco Medical Society.



KEYS, SAMUEL, Los Angeles. Died 20 February 1966, in Scottsdale, Arizona, aged 59, of acute myocardial infarction. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1932. Licensed in California in 1932. M.D. degree from California College of Medicine, 1962. Doctor Keys was a member of the Los Angeles County Medical Association.



KITIGAWA, KAY J., San Francisco. Died 6 March 1966, in San Francisco, aged 80. Graduate of Stanford University School of Medicine, Palo Alto-San Francisco, 1919. Licensed in California in 1920. Doctor Kitagawa was a member of the San Francisco Medical Society.



KONWALER, BENJAMIN EDWARD, Garden Grove. Died 27 November 1965, aged 64, of carcinoma of the stomach. Graduate of Long Island College of Medicine, New York, 1926. Licensed in California in 1944. Doctor Konwaler was a member of the Los Angeles County Medical Association.



LENTZ, JACK RAYMOND, Bakersfield. Died 20 December 1965, in Bakersfield, aged 51, of a ruptured aneurysm. Graduate of the University of Colorado School of Medicine, Denver, 1941. Licensed in California in 1947. Doctor Lentz was a member of the Kern County Medical Society.



LINTHICUM, FREDERICK HAMILTON, SR., Los Angeles. Died 28 February 1966, in San Pedro, aged 75, of heart disease. Graduate of Johns Hopkins University School of Medicine, Baltimore, Maryland, 1917. Licensed in California in 1920. Doctor Linthicum was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



MARK, BERNARD JOHN, Beverly Hills. Died 9 February 1966, in Beverly Hills, aged 56. Graduate of the University of Southern California School of Medicine, Los Angeles, 1939. Licensed in California in 1939. Doctor Mark was a member of the Los Angeles County Medical Association.



MELKONIAN, LEON, Gilroy. Died 8 August 1965, aged 64, of coronary thrombosis. Graduate of Stanford University School of Medicine, Palo Alto-San Francisco, 1927. Licensed in California in 1927. Doctor Melkonian was a retired member of the Santa Clara County Medical Society and the California Medical Association, and an associate member of the American Medical Association.

MUSFELT, W. STANLEY, Santa Ana. Died 26 February 1966, in Long Beach, aged 64, of pneumonia. Graduate of Creighton University School of Medicine, Omaha, Nebraska, 1930. Licensed in California in 1937. Doctor Musfelt was a member of the Orange County Medical Association.



PARKINSON, ROY H., San Francisco. Died 2 March 1966, in Berkeley, aged 75. Graduate of Cooper Medical College, San Francisco, 1912. Licensed in California in 1912. Doctor Parkinson was a retired member of the San Francisco Medical Society and the California Medical Association, and an associate member of the American Medical Association.



RENSHAW, R. JOHN F., Santa Ana. Died 21 November 1965, in Orange, aged 59, of carcinoma of the stomach. Graduate of the University of Oregon Medical School, Portland, 1931. Licensed in California in 1936. Doctor Renshaw was a member of the Orange County Medical Association.



ROOME, ADOLPHE EDWARD, Los Angeles. Died 20 February 1966, in Los Angeles, aged 76, of cardiovascular disease. Graduate of the Los Angeles Medical Department, University of California, 1912. Licensed in California in 1912. Doctor Roome was a member of the Los Angeles Medical Association.



ROOS, DENVER DUNBAR, Corona. Died 6 December 1965, in Riverside, aged 68, of carcinoma of the urinary bladder with metastases. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1927. Licensed in California in 1927. Doctor Roos was a member of the Riverside County Medical Association.



SNYDER, GEORGE SAMUEL, San Francisco. Died 21 February 1966, in San Francisco, aged 90. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1905. Licensed in California in 1905. Doctor Snyder was a member of the San Francisco Medical Society.



SWEELEY, MERLE E., Williams. Died 16 February 1966, in Martinez, aged 62, of heart disease. Graduate of Rush Medical College, Chicago, Illinois, 1930. Licensed in California in 1943. Doctor Sweeley was a member of the Yuba-Sutter-Colusa County Medical Society.



THURESSON, PAUL F., Riverside. Died 23 February 1966, aged 77. Graduate of Rush Medical College, Chicago, Illinois, 1915. Licensed in California in 1920. Doctor Thuresson was a member of the Riverside County Medical Association.



WARE, CHARLES WESLEY, Pasadena. Died 22 February 1966, in Pasadena, aged 63, of coronary artery disease. Graduate of Creighton University School of Medicine, Omaha, Nebraska, 1936. Licensed in California in 1938. Doctor Ware was a member of the Los Angeles County Medical Association.



## WOMAN'S AUXILIARY

to the California Medical Association

### A Word at Departure

ONE TIME a man wrote to "Dear Abby": "My wife hides my false teeth because she's afraid I'm going to step out with young girls, what can I do about it?" Abby replied, "Your wife is just being considerate of you, she doesn't want you to bite off more than you can chew."

We need people these days who are willing to bite off more than they can chew, and doctors, you married women like that! I've been reading the reports of the accomplishments of our 33 component auxiliaries, and it's amazing how much our women have achieved.

If any of you is unaware of our purpose, it is, as stated in our Bylaws, "To assist the California Medical Association in its program for the advancement of medicine and public health; and to foster friendly relations among physicians' families."

We know what a great job you men are doing. We know how busy you are now, and we know that there will be tremendously increased demands for your services, and because we want you to be able to spend some time at home with us, we're trying to see that you have more help in your profession. We sponsor Health Career days at our local high schools, showing young people by films and demonstrations how they can serve in a health career. We give scholarships to needy medical and nursing students, and raise money for AMA-ERF, for medical schools and student loans.

I've heard that some auxiliaries have had a rocking chair policy—a feeling of movement without going anywhere. But with us, that's not so. We have emphasized service this year, and we've found many ways to serve our communities. One

of our best services has also resulted in much favorable publicity—our babysitter training program. We refer to it as GEMS, which stands for Good Emergency Mother Substitutes (except when we are training boys to be Good Emergency Male Sitters). We've sponsored various safety programs—water safety, ski safety and auto safety. Many of our members have worked on programs for rural health, mental health, problems of the aging, teenage opportunities, Meals on Wheels, and various services for patients in convalescent homes. You see, doctors, your wives have not only taken a big bite in community service, we're chewing it too.

International Health Activities have extended our horizons, and tons of drug samples, books, journals, medical instruments and equipment have been sent to needy areas.

We have worked on legislation under your guidance. We've been trying to keep Medicare from doing great harm to the quality of medical care. Reminds me of a story of a farmer in Kansas who was persuaded to build a storm cellar. The storm warnings came and he took his family into the cellar, and when he came out two hours later everything was calm and peaceful—he was pretty disgusted about the storm warning. A month later storm warnings came again, and he almost had to be dragged into the storm cellar. When he emerged two hours later, he faced a complete holocaust—house gone, barn gone, nothing left standing. He surveyed the scene with awe and wonder, then nodded his head slowly and said, "Now, that's more like it!" Doctors, we don't know just what your auxiliary can do for you as you face Medicare, but your legislation committees remain ready to follow your instructions, and individually we'll listen to your complaints and comfort you as best we know how.

Last year I told you that although there occasionally may be a physician's wife who may disregard his suggestions, as an auxiliary we exist



only to please you; your slightest wish is our command—and it's been a great pleasure to me to serve your auxiliary this year.

It's been delightful serving with Dr. Teall, Dr. MacLaggan, Dr. Hosmer, Dr. Quinn and Dr. Martin, who have never been too busy to discuss auxiliary problems with me, even when I'd phone them at home. The cordial invitation of Dr. Carl Anderson to attend your Council meetings was

sincerely appreciated, and my respect and admiration for your dedicated representatives has grown each time I've had dealings with them or seen them at their work. Special thanks to Jack Collins, our staff liaison, who has been truly helpful and kind—and to all the wonderful staff of the California Medical Association. It's been a wonderful, wonderful year—thank you all.

MRS. GEORGE BOWER



# LETTERS *to the Editor*

## On "Pollen and Mold Spores—An Atmospheric and Field Survey"

THE PAPER BY SHAPIRO, Eisenberg, and Binder on "Pollen and Mold Spores—An Atmospheric and Field Survey in Los Angeles" (CALIFORNIA MEDICINE 103:340, November 1965) is open to criticism because of its many misleading statements, unwarranted conclusions, and outright errors.

The authors make it appear that theirs is the first study of this kind in the Los Angeles area. This is not so. Comprehensive botanical surveys were reported years ago by Piness, Miller, and McMinn<sup>3</sup> and by Small and Small<sup>4</sup> (this latter article is mentioned but is dismissed in a single sentence so worded as to give the impression that the Smalls' investigation was devoted primarily to pollen counts). An atmospheric pollen survey of Los Angeles has already been reported by Targow<sup>5</sup> and a survey of the atmospheric fungus spores by Targow and Plunkett.<sup>6</sup> Targow's<sup>5</sup> paper numerically and graphically shows the average monthly level of incidence for all of the important pollens in the Los Angeles area. Nowhere in the paper of Shapiro et al. is this kind of information given, contrary to what one would expect of an atmospheric survey.

The authors state that there are no clear-cut tree, grass, or weed pollen seasons in California. This statement is ambiguous. Almost any physician in Southern California can testify as to having encountered hay-fever cases who have a clear-cut season of symptoms. Perhaps what the authors meant to point out was that the pollinating period for the trees, grasses, and weeds are not as sharply separated in time here as in the East (as, roughly, spring for the trees, early summer for the grasses, and fall for the weeds); but even such a statement

could hardly be original with the authors, since the study of Piness et al.<sup>3</sup> has already shown this overlapping of pollination.

The authors state that the "importance of atmospheric mold spores in clinical allergy has been well established for many years," and then give a completely inappropriate supporting reference for this statement in place of the proper references to the work of Feinberg and of Prince.

The authors claim to have found no seasonal pattern in the atmospheric incidence of mold spores. This is contrary to reports from all over the country as summarized by Feinberg.<sup>1</sup> The latter points out that when an adequate exposure technique is used, all such atmospheric studies show a seasonal low in the incidence of *Alternaria* and of *Hormodendrum* during the winter months, then an increase in warm weather to a peak usually occurring in late summer or fall. Harsh and Allen<sup>2</sup> have shown that for a number of the fungi such peaks occur in the San Diego area in the spring. Targow and Plunkett<sup>6</sup> showed that two peaks may occur in Los Angeles for *Alternaria* and *Hormonendrum*, one in spring and one in fall.

Other criticisms of this paper can be made, such as the failure of the authors to make clear the fact that pollen of the elm tree may also be a hazard in Los Angeles in both spring and fall, as pointed out by Targow.<sup>5</sup> But enough has been pointed out to set the record straight for the most part, and to alert, for the remainder, those who in the future will have occasion to review the literature on atmospheric surveys.

WILLIS A. WINGERT, M.D.

### REFERENCES

1. Feinberg, S. M.: Allergy in Practice, 2nd ed., 1946, Chapter 7, Allergy to Fungi.
2. Harsh, G. F., and Allen, S. E.: A study of the fungus contaminants of the air of San Diego and vicinity, *J. Allergy*, 16:125, 1945.
3. Piness, G., Miller, H., and McMinn, H. E.: Botanical survey of Southern California in relation to the study of allergic diseases, *Bull. So. Calif. Acad. Sci. (Part 2)*, 25:37, 1926.



4. Small, W. S., and Small, G. M.: Botanical survey of Southern California, *Ann. Allergy*, 4:352, 1946.

5. Targow, A. M.: Pollen survey of Los Angeles, 1941-1945, *Ann. Allergy*, 6:645, 1948.

6. Targow, A. M., and Plunkett, O. A.: Fungus Allergy: I. Incidence of atmospheric spores in the Los Angeles area, *Ann. Allergy*, 9:428, 1951.

### The Authors' Reply

IN REPLY TO THE above letter, the introduction to our paper highlights the important work of Dr. Willard Small, whose report has become a standard reference for allergists in California.

Our first chart denotes the pollination times and totals per sq cm of slide area of the clinically important pollens in this area. Clinically, Chinese elm (which produces a highly toxic pollen), is most important in the fall, when it becomes a source of much trouble. Elm is not mentioned in the older works of Piness, Miller, and McMinn (1926). However, it is listed in a later work of McMinn and Maino (1963).

Our data indicate no clear-cut tree, grass, or weed seasons. In Southern California clinical allergists encounter mostly patients with multiple pollen sensitivities. However, some patients may only have symptoms during the pollination period of, perhaps, one or two species.

A discussion of the value and limitation of mold spore counts is included in our paper. Concerning this point, a personal communication from Dr. Marie B. Morrow of the University of Texas states:

"I think reports of different groups when conditions vary are good for the reading public, so they do not get the idea that air populations are static and forget that they are reflections of their sources."

The wide interest in this paper expressed by colleagues from this country and abroad has been very gratifying.

RICHARD S. SHAPIRO, M.D.  
BEN C. EISENBERG, M.D.



# INFORMATION

## Measures of Health Personnel in California

*A Report of the Bureau of Research and Planning,  
California Medical Association*

*California ranks well above average in most measures of health personnel to population, being near the top in the all-important physician/population ratio. The State also ranks high in relative numbers of nurses and of dentists.*

*Within the State, ratios of health personnel to population generally correlate with population density. The greater metropolitan areas (Los Angeles, San Francisco, and San Diego Metropolitan Areas) show the highest ratio of physicians, nurses, dentists, and pharmacists to population. Conversely, nonmetropolitan areas in California tend to have fewer health workers per person than do metropolitan areas; this is also the case in similar areas in other parts of the United States.*

*The number of physicians in California as of January 1965 is over 25 per cent greater than it was four years ago. The per cent increase has been substantially higher (33.0 per cent) outside of private practice than it has been in private practice (10.9 per cent). The increase within the private practice sector, in fact, has not quite kept pace with population growth, which has amounted to 12.6 per cent over the four-year period.*

Sources: U. S. Public Health Service *Health Manpower Source Book*, Sec. 19, "Location of Manpower in 8 Occupations," Washington, D. C., 1965; AMA Directory Report Service, *Quarterly Tables of Distribution of Physicians*, Chicago, January, 1965.

EARLIER ISSUES of Socio-Economic Report (May 1962, August 1963) have discussed the supply of

physicians in California, their distribution among the 58 counties, and physician characteristics such as type of practice and medical specialty. Information recently published by the Department of Health, Education and Welfare has provided statistics concerning all members of the health occupations, including physicians, dentists, nurses, pharmacists, sanitarians, sanitary engineers, and veterinarians. Although the data are somewhat out of date (1962) they nevertheless represent an effective measure as to the relative position of California among the 50 states in the numbers of personnel available to provide health services. This Report also presents more recent data on numbers of physicians in California.

Table 1 shows health personnel data for the United States, for four geographic regions, and for California. As can be seen, California in particular and the West in general rank considerably above the U.S. average in most ratios of health personnel to population. The difference is particularly great in the relative number of physicians to population. Noteworthy, however, is the fact that California lags behind the Northeastern region of the country in many important ratios, notably those of dentists, nurses, and pharmacists. This situation is the more unusual because it is opposite to the comparison between California and the Northeast in physician/population ratios, wherein California leads by a substantial margin.

Table 2 shows ratios of persons in health occupations to population by standard metropolitan statistical areas within California. The San Francisco-Oakland Metropolitan Area leads in most of the measures, including physicians, nurses, dentists, and pharmacists. Also well above average in physician/population ratios are the San Jose, Los Angeles-Long Beach, and the Santa Barbara Met-

TABLE 1.—Number of Health Personnel per 100,000 Population, by Region: United States, 1962

Item	United States	Region				California
		North-east	North Central	South	West <sup>1</sup>	
Dentists .....	54.1	70.3	55.5	36.9	59.8	61.2
Nurses, total .....	449.8	646.8	395.0	302.8	523.9	552.4
active .....	300.0	412.5	271.9	214.8	338.9	346.6
Pharmacists .....	66.7	80.9	65.6	54.8	69.4	63.0
Physicians, total .....	150.8	183.3	132.5	125.0	183.1	211.6
M.D. ....	142.9	176.3	122.3	121.1	170.0	195.1
D.O. ....	7.9	7.0	10.2	3.9	13.1	16.5
Sanitarians .....	5.7	4.3	4.9	6.5	8.0	6.8
Sanitary engineers .....	3.0	3.0	3.1	2.7	3.3	2.9
Veterinarians .....	11.6	7.4	15.9	10.0	13.8	11.6

<sup>1</sup>Includes California.

NOTE: The regions correspond to those used by the U. S. Bureau of the Census.



TABLE 2.—*Ratios of Persons in Health Occupations to Population, by Standard Metropolitan Statistical Areas: California, 1962*

SMSA	Ratios per 100,000 persons				
	Physicians	Active Nurses	Dentists	Pharmacists	Other <sup>1</sup>
Anaheim-Santa Ana-Garden Grove.....	176.0	333.2	52.3	59.1	18.4
Bakersfield .....	119.3	243.5	35.9	45.1	18.8
Fresno .....	138.1	257.5	48.7	57.9	24.6
Los Angeles-Long Beach.....	230.2	326.6	61.8	64.6	15.4
Sacramento .....	146.3	335.1	51.6	55.7	41.9
San Bernardino-Riverside-Ontario .....	153.7	313.3	47.0	47.7	19.5
San Diego .....	189.7	308.3	58.5	44.4	18.5
San Francisco-Oakland .....	296.2	461.5	80.4	78.5	25.0
San Jose .....	239.6	419.3	67.5	64.4	22.1
Santa Barbara .....	225.4	436.6	76.6	72.3	27.0
Stockton .....	148.4	308.6	48.3	70.3	23.3
Vallejo-Napa .....	186.0	392.6	51.6	56.9	20.5

<sup>1</sup>Includes Sanitary Engineers, Sanitarians, and Veterinarians.

ropolitan Areas. Both San Jose and Santa Barbara show high ratios of active nurses and dentists to population. The ratios of health professionals classified as "other," which includes Sanitary Engineers, Sanitarians, and Veterinarians is relatively consistent in all areas except the Sacramento Metropolitan Area; the unusually high ratio in that area is undoubtedly due to employment of personnel in these occupations by State government.

At the other end of the spectrum in physician/population ratios can be found the Central Valley areas of Bakersfield, Fresno, Stockton, and Sacramento, all of which show ratios of under 150 per 100,000 persons. Bakersfield is also well below average in ratios of nurses, dentists and pharmacists, whereas Fresno is near the average in all other ratios except nurses. The San Diego area ranks lowest in relative numbers of pharmacists.

Recent changes in metropolitan area designations should be noted. The Anaheim-Santa Ana-Garden Grove Area (Orange County) and the Vallejo-Napa Area (Solano and Napa Counties) are shown separately for the first time in this Report. Previously, the former was part of the Los Angeles-Long Beach Metropolitan Area and Solano County was included in the San Francisco-

Oakland Area. Napa County was formerly considered nonmetropolitan. Lastly, the Sacramento Metropolitan Area now includes Yolo and Placer Counties, neither of which was previously contained within any metropolitan area.

Table 3 compares ratios of persons in health occupations to population for California and the United States by type of geographic area.

The relationships among the county groups in ratios of physicians and of active nurses to population closely parallel those for the rest of the country; although higher in California than elsewhere regardless of type of area (with only one minor exception), the differences are most notable in areas termed "adjacent" and "isolated rural." In the latter category, the ratio both of physicians and of nurses is almost double that in comparable areas throughout the rest of the United States. With the exception of the health personnel classified as "other," physicians constitute the only group which shows a higher ratio to population in California than in the total United States, regardless of county group.

In all but greater metropolitan areas, dentists are relatively more numerous in California than in the remainder of the country. The higher ratios are particularly noteworthy in adjacent and in iso-

TABLE 3.—*Ratio of Persons in Health Occupations to Population, by County Group: U. S. and California, 1962*

County Group	Ratios Per 100,000 Persons									
	Physicians		Active Nurses		Dentists		Pharmacists		Other	
	U.S.	Calif.	U.S.	Calif.	U.S.	Calif.	U.S.	Calif.	U.S.	Calif.
Greater Metropolitan .....	205.0	243.5	327.5	360.8	71.0	66.4	81.2	66.1	16.2	18.4
Lesser Metropolitan .....	153.0	171.1	339.6	336.6	52.0	53.0	65.2	57.2	21.0	24.1
Adjacent to Metropolitan....	91.5	148.7	254.2	304.5	38.7	53.0	51.3	60.6	24.6	30.8
Isolated Semi-Rural .....	100.4	110.1	242.8	274.1	40.6	51.6	56.0	58.4	24.3	26.5
Isolated Rural .....	59.1	112.2	125.9	248.8	27.4	29.3	45.3	53.7	19.8	29.3

lated semi-rural counties. Pharmacists, who comprise the only major group relatively less numerous in the total State than in the nation, are, however, more abundant in all nonmetropolitan areas in California than in other states. The difference noted in greater metropolitan areas, which is of substantial proportions, is probably attributable at least in part to the distribution system in the drug field, wherein the pharmacist may in more recently developed areas of the country devote relatively more time to functioning as a pharmacist and less as a general drug clerk. The more recent rapid growth in major metropolitan areas within California explains this more efficient, specialized system of prescription drug dispensing.

The last measurement shown in Table 3 is that

of Sanitary Engineers, Sanitarians and Veterinarians to population. One can readily see that these occupations, classified together for convenience in presentation, are relatively more prevalent in California than in the rest of the United States in all types of county group.

Table 4 contains more recent (January 1965) information concerning California physicians, by selected types of practice within geographic areas. Note that these figures exclude physicians in the employ of the Federal Government.

The total number of physicians in private practice at that time was 22,674, of whom 7,707 were in General Practice (with or without part-time specialties) and 14,967 were in full-time specialties. Another 6,478 physicians were listed outside

TABLE 4.—All Non-Federal Practicing Physicians<sup>1</sup> in California, Selected Practice Data by County Medical Society Jurisdiction, January 1965

County Medical Society Jurisdiction	Private Practice			Not in Private Practice		
	Total	G.P. <sup>2</sup>	Specialist	Total	Hospital Service	All Other
CALIFORNIA TOTAL .....	22,674	7,707	14,967	6,478	4,399	2,079
Alameda-Contra Costa .....	1,856	596	1,260	457	265	192
Butte-Glenn .....	121	64	57	14	8	6
Fresno-Madera <sup>3</sup> .....	391	159	232	87	68	19
Humboldt-Del Norte .....	97	54	43	5	1	4
Imperial .....	49	23	26	8	6	2
Inyo-Mono .....	13	8	5	1	0	1
Kern .....	260	110	150	62	49	13
Kings .....	42	33	9	6	5	1
Lassen-Plumas-Modoc-Sierra .....	29	25	4	2	1	1
Los Angeles .....	9,307	3,141	6,166	2,666	1,805	861
Marin .....	304	68	236	52	34	18
Mendocino-Lake .....	65	41	24	21	18	3
Merced-Mariposa .....	64	37	27	6	4	2
Monterey .....	230	79	151	20	11	9
Napa .....	90	33	57	87	74	13
Orange .....	1,175	444	731	158	117	41
Placer-Nevada .....	86	51	35	27	23	4
Riverside .....	376	157	219	55	31	24
Sacramento-Amador-El Dorado .....	665	255	410	99	56	43
San Benito .....	9	7	2	2	0	2
San Bernardino .....	564	221	343	170	113	57
San Diego .....	1,275	475	800	189	110	79
San Francisco .....	1,774	350	1,424	1,151	822	329
San Joaquin-Alpine- Calaveras-Tuolumne .....	283	133	150	90	74	16
San Luis Obispo .....	96	40	56	35	25	10
San Mateo .....	646	124	522	95	57	38
Santa Barbara .....	327	83	244	48	30	18
Santa Clara .....	1,179	272	907	616	402	214
Santa Cruz .....	147	66	81	11	9	2
Shasta-Trinity .....	82	42	40	7	5	2
Siskiyou .....	24	17	7	1	1	0
Solano .....	112	43	69	22	12	10
Sonoma .....	219	105	114	42	31	11
Stanislaus .....	184	75	109	26	18	8
Tehama .....	23	19	4	1	1	0
Tulare .....	136	80	56	35	27	8
Ventura .....	236	113	123	87	76	11
Yolo .....	62	30	32	10	6	4
Yuba-Sutter-Colusa .....	76	34	42	7	4	3

<sup>1</sup>Excludes MD's who are retired or not in practice.

<sup>2</sup>Includes part-time specialists.

<sup>3</sup>Physicians in Madera County included with Fresno County, since a majority of those who belong to a county medical society are affiliated with the Fresno County Society.



of private practice; the majority of these (4,399) were in full-time hospital service, including internship, residency and other full-time hospital staff positions. The 2,079 physicians in the "all other" category included full-time medical school teachers, medical administrators, and physicians in laboratory medicine, preventive medicine and research. Physicians who are completely retired or otherwise not engaged in the practice of medicine are excluded from Table 4, statewide, they total 2,244 physicians.

Data for geographic areas are presented on the basis of County Medical Society jurisdictions, although the figures represent non-members as well as members. Among the 58 California counties, there are 40 medical society jurisdictions, ranging in numbers of physicians from 11 (San Benito County) to 11,973 (Los Angeles County).

In the private practice sector, the ratio of specialists is generally correlative to the degree of urbanization within an area. Among the highest ratios of specialists to all private practitioners are those in San Mateo County (522:646), San Francisco County (1,424:1,774) and Marin County (236:304). Urban areas in Southern California tend to be somewhat lower in relative numbers of specialists, in part due to the fact that former Doctors of Osteopathy who are more prevalent in the Los Angeles area are usually in General Practice. Physicians in General Practice comprise a clear majority in rural areas such as the Lassen-Plumas-Modoc-Sierra County region (25:29), Kings (33:42), Mendocino-Lake (41:65), San Benito

(7:9), Siskiyou (17:24), and Tehama County (19:23).

The ratio of physicians outside of private practice among the various areas is also of interest. Statewide, 6,478 out of 29,152 physicians are not in private practice; this amounts to slightly over one physician in five, or 22.2 per cent. Ratios vary substantially in different areas; they are highest in relatively low-population-density areas which contain a large State medical facility, such as Napa County, and in metropolitan counties where teaching hospitals are relatively prevalent, such as San Francisco. The presence of a medical school also has bearing on this situation, although not as noticeably as the other factors. Santa Clara County combines a medical school (Stanford) with a State Institution (Agnew State Hospital) and shows a ratio of physicians outside of private practice which is well above average.

In early 1961, there were a total of 18,444 M.D.'s in private practice, plus approximately 2,000 Doctors of Osteopathy in California, making a total of 20,444 physicians. This, compared with the 22,674—1965 figure, amounts to a net four-year increase of 10.9 per cent. Among physicians outside of private practice, the increase has been from 4,871 to 6,478, or 33.0 per cent. This does not account for former Osteopaths who in 1961 were engaged in a type of practice other than private practice; however, this number is assumed to have been negligible. The overall increase in practicing physicians is 15.2 per cent. During this same period, California's population has increased approximately 12.6 per cent.

693 Sutter Street, San Francisco, California 94102.



# NEWS & NOTES

NATIONAL • STATE • COUNTY

## LOS ANGELES

Modern developments in biomedical instrumentation will be reviewed by medical and instrumentation authorities at the **Fourth National Biomedical Instrumentation Symposium**, 16 to 18 May, at the Disneyland Hotel, Anaheim.

Sponsored by the Instrument Society of America, the meeting has received special endorsement from the California Medical Association, the Orange County Medical Association and the Los Angeles County Medical Association.

Six half-day sessions will cover topics of mutual interest to the medical and measurement professions and it is planned for appeal to clinicians, diagnosticians, educators, pathologists, intensive care specialists, anesthesiologists, physiologists and life-support scientists.

\* \* \*

The University of Southern California has received from the Public Health Service a five-year grant totaling more than \$650,000 for **graduate education and research in the field of aging**.

The goal is to produce experts in various specialties who will be capable of original research and teaching, and who will fill national leadership responsibilities in the ensuing decades.

Funds are immediately available to support qualifying students who want to make a career in the field of gerontology while pursuing graduate studies in a special aspect of aging.

\* \* \*

Dr. W. Ballentine Henley, provost of the **University of California, California College of Medicine**, has announced the following new **faculty appointments** for UC-CCM, made upon recommendation of Dean Warren L. Bostick:

**Pathology**—Elmer R. Jennings, M.D., as clinical professor and Stephen Lee, M.D., clinical associate; **Psychiatry and Human Behavior**—Paul V. Gustafson, M.D., clinical instructor; **Ophthalmology**—James M. McCaffery, M.D., clinical instructor; **Urology**—Russell T. Bergman, M.D., associate clinical professor; **Gynecology and Obstetrics**—Stanley R. M. Zerne, M.D., associate clinical professor; **Medicine (Neurology)**—Leslie B. Mann, M.D., associate clinical professor; **Surgery**—Sanford A. Hepps, M.D., clinical instructor; **Orthopedic Surgery**—Arthur Brody, M.D., as clinical instructor and Iqbal Singh, M.D., as assistant clinical professor.

## SAN DIEGO

The San Diego County Medical Society will participate in a long-range **community program to reduce cigarette smoking** in the first experiment of its kind in the United States.

The program will be supported by the Public Health Service's National Clearinghouse for Smoking and Health, it was announced by Dr. Daniel Horn, Clearinghouse director.

The San Diego County Council on Smoking and Health, through a contract awarded to the County Medical Society, a member organization, will undertake the initial planning of a county-wide five year program to test methods by which organized community action can control cigarette smoking through public education and mass media. Project director will be Dr. Arnold L. Flick, a representative of the county medical society.

## YOLO

Dr. Earl F. Wolfman, Jr., of the University of Michigan has been named associate dean of the **School of Medicine at the University of California, Davis**. The new associate dean, whose appointment is effective 1 July, also will serve as professor of surgery and chairman of the division of surgery.

Dr. Wolfman is the second member of the new medical school at Davis. Dr. John Charles Tupper was appointed dean earlier this year. Additional faculty will be added during the coming months, said Dean Tupper, and plans are under way for temporary and permanent quarters for the school in preparation for the first students in 1968.

## GENERAL

The California Research and Medical Education Fund of the Tuberculosis and Health Association of California has invited applications for **research grants** for 1966-67 in clinical, social, epidemiological, laboratory, and related fields of investigation of **tuberculosis and other respiratory diseases**. The announcement said that the fund particularly wishes to encourage young investigators.

Deadlines for applications for 1966-67 are: 1 May 1966 and 1 November 1966.

Further information and application forms may be obtained from: Tuberculosis & Health Association of California, 424 Pendleton Way, Oakland, California 94621.

\* \* \*

At the sixteenth annual meeting of the **California Society of Plastic Surgeons** held at Palm Desert, California, 17 to 19 March, the following officers were elected: President, Dr. Charles F. Steiss, San Francisco; president-elect, Dr. Kathryn L. Stephenson, Santa Barbara; vice-president, Dr. Henry S. Patton, Oakland; secretary-treasurer, Dr. William J. Morris, San Francisco.



# EDUCATION NOTICES

## Meetings and Courses

### COMMITTEE ON CONTINUING MEDICAL EDUCATION

THIS BULLETIN of the dates of continuing education programs and the meetings of various medical organizations in California is supplied by the Committee on Continuing Medical Education of the California Medical Association. In order that they may be listed here, please send communications relating to your future meetings or postgraduate courses to Committee on Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco, California 94102.

#### KEY TO ABBREVIATIONS AND SYMBOLS

##### Medical Centers and CMA Contacts for Postgraduate Course Information

- CMA:** California Medical Association  
For information contact: Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco 94102. PRospect 6-9400, Ext. 68.
- LLU:** Loma Linda University  
For information contact: W. F. Norwood, Ph.D., Associate Dean, Continuing Education, Loma Linda University School of Medicine, 1720 Brooklyn Ave., Los Angeles 90033, ANgeles 9-7241, Ext. 214.
- PRES. MED. CTR.** Presbyterian Medical Center  
For information contact: Arthur Selzer, M.D., chairman, Education Committee, Presbyterian Medical Center, Clay and Webster Streets, San Francisco 94115. WEst 1-8000.
- UCLA:** University of California at Los Angeles  
For information contact: Donald Brayton, M.D., Assistant Dean for Postgraduate Medical Education, 15-39 Rehabilitation Center, University of California Center for Health Sciences, Los Angeles 90024, 478-9711, Ext. 4345.
- UCSF:** University of California, San Francisco  
For information contact: Seymour M. Farber, M.D., Dean, Educational Services and Director, Continuing Education, University of California Medical Center, Room 565-U, San Francisco 94122, 666-1692.
- USC:** University of Southern California  
For information contact: Phil R. Manning, M.D., Associate Dean, Postgraduate Division, USC School of Medicine, 2025 Zonal Ave., Los Angeles 90033, CApital 5-1511, Ext. 300.
- STAN:** Stanford University  
For information contact: Roy Cohn, M.D., Associate Dean for Graduate Affairs, Stanford University School of Medicine, 300 Pasteur Drive, Palo Alto, DAVenport 1-1200.

#### APRIL

- April 16—Ankle Injuries in Athletics. UCLA. Saturday. 6 hours. \$25.
- April 16-17—The Uncertain Quest: The Teen-Ager's World. UCSF. Saturday-Sunday. 12¾ hours. \$15.
- April 19-May 24—San Francisco Academy of General Practice Postgraduate Medical and Surgical Clinics. French Hospital, San Francisco. Tuesdays. \$20 members, \$25 non-members. Contact: Rafael P. Bricca, M.D., 909 Hyde Street, San Francisco.
- April 22-23—Pediatrics and Pediatric Surgical Presentations. Amphitheater Conference Room, Children's Hospital of Orange County, 1109 West La Veta, Orange 92666. Friday-Saturday. Contact: Merl J. Carson, M.D., Medical Director, CHOC.
- April 23 — Southern California Psychiatric Society Spring Meeting. Statler Hilton Hotel, Los Angeles. Saturday. Contact: Ralph M. Obler, M.D., chairman, SCPS, 9629 Brighton Way, Beverly Hills.
- April 23-24—Mental Retardation and Emotional Disturbance in Childhood and Adolescence. UCSF at Sutter Memorial Hospital, Sacramento. Saturday-Sunday. 9½ hours. \$7.
- April 25-27—Annual Meeting of the Council on Medical Television. UCSF. Monday-Wednesday. 20 hours. \$15 members, \$20 non-members.
- April 28-29—General Surgery. UCSF. Thursday-Friday. 12½ hours. \$60.
- April 28-30—REDWOOD REGIONAL CONFERENCE presented by California Medical Association in cooperation with USC. Konocti Harbor Inn, Clear Lake. Thursday noon-Saturday noon. \$15. "Cardiovascular Disease, Endocrinology, Office Techniques in Patient Interviews." Chairman: Lucius L. Button, M.D., 1102 Montgomery Drive, Santa Rosa.
- April 30—Recent Advances in Infant Cardiology. USC at Children's Hospital of Los Angeles. Saturday. 7 hours.
- April 30-May 1—Clinical Considerations in Mental Retardation. UCSF at Sonoma State Hospital, Eldridge. Saturday-Sunday. 10¾ hours. \$10.

#### MAY

- May 1-5—American Society for Microbiology. Biltmore Statler Hilton Hotel, Los Angeles. Sunday-Thursday. Contact: R. W. Sarber, executive secretary, 115 Huron View Blvd., Ann Arbor, Michigan.
- May 3-6—American College Health Association. El Cortez Hotel, San Diego. Tuesday-Friday. Contact: Benjamin R. Reiter, M.D., executive director, University of Miami, Bldg. 37-X, 1200 Dickinson Drive, Coral Gables, Florida 33146.
- May 5-7—Ear, Nose, Throat. UCSF. Thursday-Saturday. 18 hours. \$50.
- May 5-26—Neuropsychiatric Management in Daily Practice. UCSF at Modesto State Hospital, Modesto. Thursdays. 8 hours. \$7.
- May 6—Symposium on Hypertension. USC at Statler Hilton Hotel, Los Angeles. Friday. 7 hours.
- May 7—Ventura County General Hospital Annual

- Staff Seminar.** VCGH. Saturday. 6 hours. No fee. Contact: G. K. Ridge, M.D., VCGH, 291 Loma Vista Road, Ventura.
- May 7-8—Dynamic Measurements with Radioisotope Techniques for Evaluating Organ Function and Circulation.** UCLA. Saturday-Sunday.
- May 7-8—Seminar on Chronic Respiratory Problems.** Lebanon Hall, Cedars of Lebanon Hospital, 4833 Fountain Avenue, Los Angeles. Saturday-Sunday. 12 hours. \$15. Contact: Mr. Seymour P. Stein, seminar coordinator, Ben R. Meyer Rehabilitation Center, CLH.
- May 11—American Cancer Society Scientific Session.** St. Francis Hotel, San Francisco. Wednesday. Contact: Lewis W. Guiss, M.D., 1930 Wilshire Blvd., Los Angeles 90057.
- May 12-15—Hawaii Medical Association Annual Meeting.** Arthritis and Psychiatry. Princess Kailuani Hotel, Honolulu. Thursday-Sunday. 15 hours. \$35. Contact: Miss Lee McCaslin, executive secretary, 510 S. Bere-tania, Honolulu, Hawaii 96813.
- May 13-14—SAN JOAQUIN VALLEY COUNTIES—Regional Postgraduate Institute presented by California Medical Association in cooperation with UCLA.** Ahwahnee Hotel, Yosemite. Friday-Saturday. \$15. "Cerebral and other Vascular Diseases, Head-ache." Chairman: Dale Kirkegaard, M.D., 2432 Cala-veras Street, Fresno.
- May 14—Humboldt-Del Norte Medical Society Annual Medical Symposium: "Frontiers in Medicine."** Eureka Inn, Eureka. Saturday. 4 hours. Contact: Stanwood S. Schmidt, M.D., president, 707 K Street, Eureka.
- May 14-15—Hypnosis, A Critical Evaluation.** UCSF at Napa State Hospital, Imola. Saturday-Sunday. 12 hours. \$10.
- May 16-18—National Biomedical Instrumentation Sym-posium.** Sponsored by Instrument Society of America. Disneyland Hotel, Anaheim. Monday-Wednesday. \$20: members of ISA or AMA, \$25: others. Contact: Thomas B. Weber, M.D., Beckman Instruments, Inc., 2500 Harbor Blvd., Fullerton.
- May 18—Peripheral Vascular Disease.** USC. Wednes-day. 7 hours.
- May 19—California Heart Association Annual Scien-tific Session.** Ambassador Hotel, Los Angeles. Thurs-day. 6 hours. No fee. Contact: Arthur Feinfeld, M.D., CHA, 1370 Mission Street, San Francisco.
- May 20-21—San Diego Academy of General Practice Annual Postgraduate Symposium presented in co-operation with University of Oregon School of Medicine.** Vacation Village Hotel, Mission Bay, San Diego. Friday-Saturday. Contact: Orlando P. Johann, M.D. 731 E. Broadway, El Cajon.
- May 20-21—Pain.** UCSF. Friday-Saturday. \$40. 10½ hours.
- May 20-22—Complications in Modern Medical Prac-tice.** UCLA. Friday-Sunday. 18 hours.
- May 21—"Clinic Day"—Diseases of Medical Progress.** Channing House Auditorium, Palo Alto. Saturday. 9:00 a.m. to 3:30 p.m. Contact: R. Hewlett Lee, M.D., Palo Alto Medical Clinic, 300 Homer, Palo Alto.
- May 23-25—American Thoracic Society Annual Meet-ing.** Hilton Hotel, San Francisco. Monday-Wednesday.
- Contact: James Kieran, M.D., chairman, Medical Ses-sions Committee, American Thoracic Society, 1790 Broadway, New York, N.Y. 10019.
- May 28-June 29—Medical Centers of Europe.** USC. 50 hours. \$250.
- May 20-21—San Diego Academy of General Practice Annual Postgraduate Symposium** in cooperation with University of Oregon School of Medicine. Vac-a-tion Village Hotel, Mission Bay, San Diego. Friday-Saturday. Contact: Orlando P. Johann, M.D., 731 E. Broadway, El Cajon.

## JUNE

- June 10-11—Convulsive Disorders.** UCSF. Friday-Sat-urday.
- June 11-12—The Drug Takers.** UCLA. Saturday-Sun-day. 12 hours.
- June 11-12—Orthopaedic Problems in the Adult.** Leba-non Hall, Cedars of Lebanon Hospital Division, 4822 Fountain Avenue, Los Angeles. Saturday-Sunday. \$15. Contact: Alex Evelove, director, Cedars-Sinai Medical Center, 8720 Beverly Blvd., Los Angeles 90048.
- June 16-19—California Society of Anesthesiologists Biennial Scientific Meeting.** Sahara Tahoe Hotel, South Shore, Lake Tahoe. Thursday-Sunday. \$25. Contact: Mr. Norman R. Catron, executive secretary, CSA, 39 North San Mateo Drive, San Mateo 94401.
- June 17—Attending Staff Association of Olive View Hospital Symposium on Infectious Diseases.** OVH, Olive View. Friday. Contact: Joseph K. Indenbaum, M.D., secretary-treasurer, ASAOVH, Olive View.
- June 18—Diagnosis and Management of Infectious Diseases.** Amphitheater Conference Room, Children's Hospital of Orange County, 1109 W. La Veta, Orange 92666. Saturday. 8:30 a.m. to 4:00 p.m. \$5 (lunch included). Contact: Merl J. Carson, M.D., Medical Director, CHOC.
- June 22-24—Highlights of Modern Ophthalmology.** Lions Eye Bank. Wednesday-Friday. 8 hours daily. \$75. Contact: Eva del Oro, secretary, Lions Eye Bank, 2018 Webster Street, San Francisco.
- June 22-24—Treatment of Fractures.** USC. Wednesday-Friday.
- June 23-25—SACRAMENTO VALLEY COUNTIES—Regional Postgraduate Institute presented by Cali-fornia Medical Association in cooperation with Stanford.** Harvey's Resort Hotel, Lake Tahoe. Thurs-day noon-Saturday noon. \$15. "Advances in Therapy: Diseases of Medical Progress, Newer Antibiotics, Pep-tic Ulcer Disease, Cosmetic Plastic Surgery." Chair-man: John N. Miller, Jr., M.D., 5301 F Street, Sacra-mento.

## AUGUST

- August 28—American Association of Electromyogra-phy and Electrodiagnosis.** Sheraton-Palace Hotel, San Francisco. Sunday. Contact: Max Karl Newman, M.D., director, 16861 Wyoming Avenue, Detroit 48221.
- August 28-September 2—American Academy of Physi-cal Medicine and Rehabilitation.** Sheraton-Palace Hotel, San Francisco. Sunday-Friday. Contact: Harriet E. Gillette, M.D., secretary, Cleveland Clinic, Clevel-land.



## SEPTEMBER

September 8-10—**Saint John's Hospital Annual Postgraduate Assembly.** SJH, 1328 22nd Street, Santa Monica. Thursday-Saturday. Contact: John C. Eagan, M.D., director, SJH.

September 17—**Annual Symposium on Cardiovascular Disease.** Sponsored by the Santa Barbara County Heart Association. Biltmore Hotel, Santa Barbara. Saturday. 6 hours. \$12.50. Contact: Sara Clyde, executive director, 18 La Arcada Court, Santa Barbara.

September 25-26—**Annual San Francisco Cancer Symposium.** "High Energy Electrons in the Treatment of Cancer." Sponsored by Claire Zellerbach Saroni Memorial Tumor Institute. Sunday-Monday. 10 hours. \$25. Contact: Jerome M. Vaeth, M.D., director, STI.

September 26—**Society for Pediatric Radiology.** Hilton Hotel, San Francisco. Monday. Contact: John L. Gwinn, M.D., treasurer, Children's Hospital, 4614 Sunset Blvd., Los Angeles 90027.

September 27-30 — **American Roentgen Ray Society.** Hilton Hotel, San Francisco. Tuesday-Friday. Contact: C. Allen Good, M.D., executive secretary, Mayo Clinic, 200 First Street, SW, Rochester, Minn. 55901.

September 28-30—**Annual Postgraduate Symposium on Heart Disease.** Sponsored by San Francisco Heart Association. St. Francis Hotel, San Francisco. Wednesday-Friday. 18 hours. \$35. Contact: Gene C. Taylor, executive director, SFHA, 259 Geary Street, San Francisco.

September 28-30—**American Association of Medical Clinics.** Hotel Del Coronado, San Diego. Wednesday-Friday. Contact: Edwin P. Jordan, M.D., executive director, P.O. Box 58, Charlottesville, Va. 22902.

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# The Physician's BOOKSHELF

**SURGERY OF THE FOOT—Second Edition—**Henri L. DuVries, B.S., D.S.C., M.D., Assistant Clinical Professor of Orthopaedic Surgery, University of California School of Medicine; Associate Orthopaedic Surgeon, University of California Medical Center, San Francisco; in collaboration with Members of the Faculty of the University of California School of Medicine, San Francisco. Foreword by Verne T. Inman, A.B., M.A., Ph.D., M.D. The C. V. Mosby Company, St. Louis, Mo., 1965. 586 pages, \$17.50.

This is a delightful book to read, informative, authoritative, detailed and beautifully illustrated. However, where the reader may breathe a fervent "Amen" to some sections, to others he will explode, "How can anyone be so misinformed." The book gathers in accessible arrangement much useful information on the foot, presenting it interestingly, frequently provocatively, occasionally infuriatingly. The reader will be offended by the statement "The human foot has been neglected during the past hundred years" . . . which casts needless opprobrium on the painstaking efforts of conscientious workers who preceded the author in this field.

An enlargement of, and marked improvement over, the first edition, this encyclopedic compendium gains further stature from the competent authors Dr. DuVries has invited to write chapters appropriate to their special interests.

One of the joys of reading this text lies in positive and uncompromising stands Dr. DuVries takes on controversial subjects. A vigorous advocate of his own surgical procedures, and an outspoken critic of others in common use today, the author supports his contentions with dramatic x-rays illustrating the bad results achieved by the operations he decries. Hallux valgus, bunions, plantar keratoses, and their operative corrections are especially profitable reading.

Dr. Larson's section on fixed deformities of the foot is clear, concise, and practical. From his wealth of experience, he has boiled down the past fifty years' accumulation of operations into the handful which he finds helpful. A few redundancies slow the reading. Could not at least one of the thirteen x-rays of subungual exostoses have been omitted?

In the interest of accuracy and completeness, certain minor changes might appear in the inevitable third edition. Dr. Lantzonis would turn over in his grave at the casual misrepresentation of his ingenious and often successful operation for cock-up deformity of the fifth toe. A short analysis of the source and growth of the nail and nail bed would clarify the rationale for successful toenail surgery. Many of us would profit from hearing how Dr. DuVries managed the 30 per cent unsuccessful results from 400 operations he did for plantar keratoses.

This text will prove exciting reading for any foot healer, be he a medical student paring a plantar wart, the occasional toenail dabbler who cannot understand why a margin nail-spur recurs every time he operates on an ingrown toenail, the internist whose curiosity is aroused by the vascular implications of a glomus tumor, an orthopedic resident who questions the wisdom of resection of the metatarsal head for Freiberg's infraction, or the self-assured orthopedist who for years has been satisfied with Keller's repair of hallux valgus.

Space does not allow the reviewer to make even a small fraction of the comments he would like—both positive and negative; however, his reaction is best expressed by saying that he will add this book to his library for re-reading and ready reference.

## REFERENCES

1. L. A. Lantzonis: Congenital subluxation of the fifth toe, *J. of Bone & Joint Surg.*, January 1940, Vol. XXII:1, pp. 147-150.
2. Barton L. Lewis: Microscopic studies of fetal and mature nail and surrounding tissues, *Arch. Dermatol.*, Vol. 71, 1954.

ROBERT P. WATKINS, M.D.

\* \* \*

**GASTROENTEROLOGY—Volume III, Second Edition—**Henry L. Bockus, M.D., Emeritus Professor of Medicine, University of Pennsylvania Graduate School of Medicine; and present and former colleagues at the University of Pennsylvania Graduate School of Medicine and School of Medicine. W. B. Saunders Company, Philadelphia, Pa., 1965. 1352 pages, \$30.00.

Volume III of Bockus' Gastroenterology has now appeared to complete the extensive revision of this standard work. Parasitic disease, the liver, affections of the gall-bladder and bile ducts, the pancreas and secondary affections of the gastrointestinal tract and miscellany are the section titles and as in the previous volumes of this second edition, these subjects are discussed from the standpoint of the clinician.

Of particular interest are the chapters on psychiatric aspects of gastrointestinal function and disease, on intimations of autoimmunity in digestive disease, on gastrointestinal allergy, collagen disease, abdominal vascular disease, food poisoning and on interrelationships of the gastrointestinal tract and the cardiovascular, endocrine, genitourinary and dermatologic systems.

The material is very well presented in detail and in readable fashion maintaining the high standard established in the previous volumes. Large and lucid illustrations, including those of radiologic films and photographs, have been extensively used to supplement the text and stimulate the interest and satisfy the curiosity of the reader. Again physiologists, biochemists and pathologists who want a better understanding of the clinical relations of their fields of interest in gastroenterology as well as internists, surgeons, radiologists, in fact all physicians, will find much of sound background and practical usefulness in these pages.

The extensive and excellent bibliography at the end of each chapter will enable the student or physician to pursue further the original sources of much of the work in gastroenterology not only of Bockus and his group but also of most authorities in the field.

Considering all three of the volumes of this outstanding work one cannot help but admire the accomplishments and persistence of the author in presenting for the whole profession in such a clear and lucid way the tremendously rapid developments in the ever widening field of gastroenterology as he and his "school" have experienced them in the clinic, in the laboratory and in the care of the patient.



**THE ESSENTIALS OF ROENTGEN INTERPRETATION—Second Edition**—Lester W. Paul, M.D., Professor of Radiology, The University of Wisconsin Medical School; and John H. Juhl, M.D., Professor of Radiology and Chairman of the Department of Radiology, The University of Wisconsin Medical School. Hoeber Medical Division (Harper & Row, Publishers, Inc.), New York, 1965. 902 pages, \$25.00.

The second edition of this comprehensive work appears approximately six years after the first. It remains divided into six main sections, dealing respectively with the osseous system, the central nervous system, the gastrointestinal system, the genitourinary system, the chest and finally, the face, mouth and jaws.

The text is slightly expanded over that of the first edition, and more than 100 new illustrations of excellent quality have been added. Amongst the new additions to this volume are considerations of genetic syndromes, renal vascular problems and rarer bone disorders. Every chapter has been rewritten. The index is adequate. The text can be recommended to the student and the practitioner.

L. HENRY GARLAND, M.D.

\* \* \*

**VIRAL AND RICKETTSIAL INFECTIONS OF MAN—Fourth Edition**—Edited by Frank L. Horsfall, Jr., M.D., Sloan-Kettering Institute for Cancer Research; and Igor Tamm, M.D., The Rockefeller Institute. J. B. Lippincott Company, Philadelphia, Pa., 1965. 1282 pages, \$15.50.

This companion volume to the recent new (fourth) edition of "Bacterial and Mycotic Infections of Man," is intended to "make readily available comprehensive information about viruses, rickettsiae, and the infections they induce." Six years have elapsed since the last (third) edition of "Viral and Rickettsial Infections of Man," and the amount of new information accumulated in that interval is staggering. To do partial justice to new developments, a whole series of new chapters has been added to deal with the architecture and chemistry of virus particles, the biochemistry of viral replication and its inhibition, and new insights into virus-cell interactions. Most of these new features, prepared by distinguished investigators in a discriminating fashion, make excellent reading.

The bulk of the volume's 1,200 pages covers individual groups of viruses, their characteristics, the diseases and the epidemiologic patterns they produce. That section provides a useful source of reference for physicians, teachers and investigators, but for the harried medical student there is probably too much detail (e.g., what student *really* wants to read 100 pages on arboviruses!).

Clearly, the editors are caught in a serious dilemma. On the one hand, they wish to present the exciting, vital new aspects of viruses which are at the center of cell biology, molecular genetics, oncogenesis, etc. On the other hand, they feel obliged to adhere to the title and stress infections of MAN, focusing on clinical and epidemiologic features. There is the further problem of the traditional inclusion with viruses of agents of the psittacosis-trachoma group and rickettsiae. Actually, these disease-producing agents are closely related to intracellular bacteria rather than to viruses and, consequently, the last 200 pages of the book have little connection with the fundamental information on viruses presented in the first 300 pages!

In spite of these drawbacks, and the 20-month delay between the preparation of manuscripts and their appearance in print, this volume is an excellent source of reference and should be found on many library shelves.

ERNEST JAWETZ, M.D.

**ADVANCES IN BLOOD GROUPING II**—Alexander S. Wiener, M.D., F.A.C.P., Senior Bacteriologist (Serology) to the Office of the Chief Medical Examiner of New York City, Adjunct Associate Professor of the Department of Forensic Medicine of the New York University Medical School, and Attending Immunohematologist to the Jewish and Adelphi Hospitals of Brooklyn, N.Y. With a section by Maurice Shapiro, M.B., B.Ch., F.C.Path., Director, The South African Blood Transfusion Service; Honorary Lecturer in Immunohaematology, University of the Witwatersrand, Johannesburg, South Africa. Grune & Stratton, Inc., New York, 1965. 454 pages, \$12.50.

This is the third volume of collected reprints of journal articles by this author, each containing a different selection. The introductions and discussions of many of the papers repeat the same statements again and again, and it is regrettable that the author chooses to present material in this fashion. The voluminous literature on blood grouping makes it difficult for anyone to read all of it, so that material which is unnecessarily repetitious is particularly annoying.

The author makes it quite clear that he has two purposes in preparing this volume. Foremost is his desire to convince the reader that his own genetic interpretations and nomenclature should be utilized exclusively and that the Fisher-Race nomenclature for the Rh system be completely abandoned. It becomes increasingly evident that Wiener's interpretation of the genetics of the Rh system may be the correct one, but his prolific arguments on the subject of nomenclature have been excessive to the point of doing himself a disservice. The second motive for the publication of this volume is to remind the readers of areas in which the author deserves recognition for the priority of various discoveries. This leads to the regrettable inclusion of a 1949 article on the pathogenesis of erythroblastosis fetalis in which he called attention to the importance of intravascular sludging of red cells. Unfortunately the article largely concerns itself with a comparison between erythroblastosis fetalis and the Schwartzman phenomenon, and the discussion of the latter is completely at variance with current theory.

On the other hand, Wiener's genius and the importance of his contributions cannot be denied. Many workers in the field of blood grouping will be pleased to have a number of his important papers readily accessible on their library shelves in a book form.

HERBERT A. PERKINS, M.D.

\* \* \*

**ESSENTIALS OF GYNECOLOGY—Third Edition**—E. Stewart Taylor, M.D., Professor and Chairman of the Department of Obstetrics and Gynecology, University of Colorado School of Medicine, Denver, Colorado. Lea & Febiger, Philadelphia, 1965. 603 pages, \$15.00.

Present day medical pedagogy has need of a small, current textbook of gynecology for those students who plan to specialize in nongynecological fields, which unfortunately includes about 99 per cent of most senior classes. Taylor's new edition of *Essentials of Gynecology* is well organized, current and relatively small. Like its predecessors it will continue to be popular with medical students. The chapters on stress incontinence, adrenal gland in gynecology, primary gonadal failure, and physiology and endocrinology of the female generative tract are fresh, succinct and authoritative. Throughout the entire book, the historical aspects of gynecology are emphasized and the bibliographies, though brief, are well chosen.

In many sections, in an obvious effort to mention all topics, the discussions tend to be superficial and frequently there is minimal distinction between the common and the rare. Exfoliative cytology is almost totally ignored and while not every text can include a compre-



hensive discussion of cytopathology, the subject is one of the more rapidly changing and important in all of gynecology.

The book is nicely published and its many illustrations are of excellent quality and clarity. If the book sold for about half of its listed price, it would be strongly recommended to all medical students.

ROBERT C. GOODLIN, M.D.

\* \* \*

**GENERAL ANESTHESIA—**Volumes 1 and 2, Second Edition—Edited by Frankis T. Evans, M.B., B.S., F.R.C.S., F.F.A.R.C.S., Anaesthetist, St. Bartholomew's Hospital, St. Mark's Hospital for Rectal Disease, and Royal Masonic Hospital, London; and T. Cecil Gray, M.D., F.F.A.R.C.S., Professor of Anaesthesia, University of Liverpool. Volume 1—Basic Principles; Volume 2—Clinical Practice. Butterworth Inc., Washington, D.C., 1965. 1,376 pages, illustrated, \$39.50 per set.

This two-volume work is edited by two British anesthetists. The book has multiple authors. It is the second edition and contains a total of 1300 pages.

Volume I is concerned with "Basic Principles" and Volume II with "Clinical Practice."

Much of the information is already outdated as predicted by the authors. Many of the authors are not anesthetists and, as a result, fail to emphasize items and areas of significance to the practicing anesthetist. For example, the chapter on Anatomy does not devote itself primarily to those aspects of anatomy in which the anesthetist is most interested. The organization is such that an anesthetist might find it easier to refer to a standard anatomical text or an atlas.

Throughout the text, terms are used which are peculiar to England. Many drugs are discussed and British trade names or generic terms used exclusively. For United States readers, it would have been helpful to have USA generic terms included, at least, parenthetically.

Many dogmatic and unqualified statements are made about items anent which there is difference of opinion. For example, "at normal atmospheric pressure raising the oxygen in the inspired air to 60 per cent for longer than twelve hours will cause irritation of the respiratory tract with coughing and substernal pain." It is also stated that "it may be concluded from the evidence available that at halothane concentrations of 2 per cent and below, there is no significant depression of myocardial function."

As a reference text, these volumes may be useful to provide relatively up-to-date information on most any topic of interest to the anesthetist. It will still be necessary for the anesthetist to explore other sources for more recent and broader data.

\* \* \*

**THERAPEUTIC RADIOLOGY—**Rationale, technique, results—Second Edition—William T. Moss, M.D., Professor of Radiology, Northwestern University School of Medicine, Department of Radiology, Chicago, Illinois; Director, Department of Therapeutic Radiology, Veterans Administration Research Hospital, Chicago, Illinois. With foreword by Lauren V. Ackerman, M.D. The C. V. Mosby Company, St. Louis, 1965. 514 pages, \$18.75.

This edition appears approximately six years after the first, and is enlarged about 25 per cent.

The opening chapters discuss basic principles and remain in general sound. Subsequent chapters show a tendency in some sites to recommend megavoltage over orthovoltage despite the absence of any valid statistical evidence for improved cure rates.

It is to be hoped that the next edition will contain reference to the only large controlled study of orthovoltage and supervoltage, that conducted by Paterson and associates in Manchester during the last decade. This study

showed that in cancer of the cervix, Stages I to III, the survival rate following a combination of orthovoltage and intracavitary radium was significantly higher than that using a combination of megavoltage and intracavitary radium. Further, mention should be made in the next edition of the fact that Kottmeier, after several years' use of telecobalt returned to orthovoltage as a supplementary radiation in the more advanced stages of cancer of the cervix, because of the smaller number of undesirable bowel effects.

The illustration on page 231 shows a telecobalt beam used for irradiating the internal mammary nodes in females with cancer of the breast. It should be added that this technique has been abandoned by several authors on account of undesirable deep effects. These authors now use orthovoltage for such irradiation, when it is indicated.

References are appended to each chapter and there is a good index.

\* \* \*

**CLINICAL ANTICOAGULANT THERAPY—**I. Myron Vigran, M.D., M.S. (in Med.)—Fellow, American College of Physicians, American College of Cardiology, American College of Chest Physicians and International College of Angiology; Associate Attending Physician, Cedars of Lebanon Hospital; Associate Physician, Mount Sinai Hospital, Los Angeles, California; Director, Research Foundation for Circulatory Disease, Beverly Hills, California; formerly Instructor in Medicine, University of Southern California; with collaborating authors and a foreword by Irving S. Wright. Lea & Febiger, Philadelphia, Pa., 1965. 315 pages, \$15.00.

This is a delightful and, at the same time, scholarly book, which covers well the indications, contraindications, usage and complications of anticoagulant drug therapy. The historical introduction and chronology of the development of such therapy, plus the other concise compilations of knowledge to the present, follow the best medical tradition in collating knowledge: observe, record, tabulate.

There is a good chapter on the advantages and disadvantages of the various laboratory tests used to control anticoagulant therapy. Although the author has previously shown his own preference for the thrombotest, he gives a thorough and unbiased evaluation of the other tests as well. Despite its disadvantages, the Quick one-stage test still remains the most widely used laboratory control.

While the author's sample instruction sheet for patients is excellent, this reviewer believes that the patient beginning anticoagulant therapy must be given thorough office instruction concerning the recognition and differentiation of minor and serious bleeding episodes. Those patients who cannot be taught these points probably should not be treated on a long-term basis. These careful verbal precautions would probably obviate the need for the author to over-emphasize the danger of bleeding in his printed instructions.

Such experts as Ellen McDevitt and Arnold G. Ware have written excellent chapters regarding their particular fields of knowledge. Also the inclusion of photographs and biographical data of the outstanding men contributing to the development of this therapy—McLean, Best, Link, Owren and Wright, among others—adds an additional fillip.

Nearly every phase of anticoagulation is covered in this book, all in a very readable format. There are some minor deficiencies in bibliographic acknowledgments, but for the most part, the references are complete.

For any physician using anticoagulant drug therapy, this is a worthwhile reference book.



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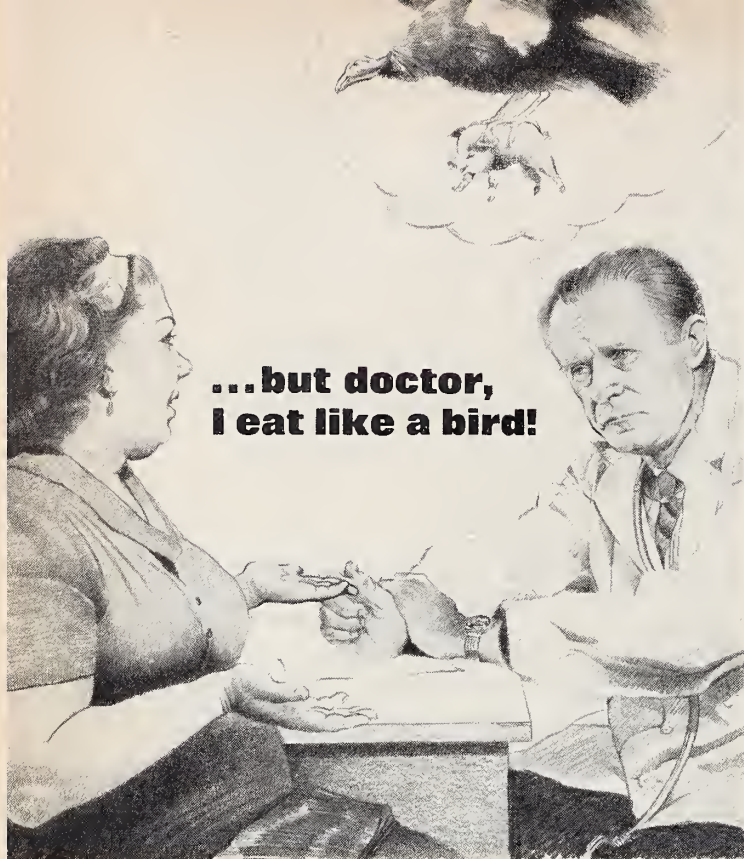
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### **Private Physicians Needed in Research**

Today's medical research needs more aid from the physician in private practice, says a senior editor of the *Journal of the American Medical Association* in the February 14 issue.

The trend of modern research, however, is to a highly specialized, subdivided team effort. Where does the private physician fit in?

The doctor—and his patients—already have an important role in clinical investigations, particularly in the evaluation of new drugs. They are needed for even more of these investigations, said Alfred Soffer, M.D.

The practicing physician also could work with investigators studying environmental or genetic aspects of disease, he suggested.

"He should be welcomed as a part of investigational teams," Dr. Soffer said. "The unique relationship between physician and patient can be utilized for long-term studies in the natural courses of numerous diseases."

In addition, the physician should be able to do research in his own locality. The community hospital with an adequate full-time staff is a good site for encouraging research and publication, Dr. Soffer said.

Once the practicing physician becomes a researcher-author of medical literature, he also becomes a more critical reader of medical literature, Dr. Soffer suggested.

Important groups of specialists are needed to help the private physician in his research.

"The services, for example of biostatisticians and clinical pharmacologists are frequently not utilized and indeed are apparently not available in a significant number of academic centers," Dr. Soffer said.

Where such specialists are in short supply, particularly in non-university localities, community hospitals might cooperate to build a staff of research consultants. These then could be "loaned" to local physicians engaged in research, Dr. Soffer suggested.

The specialists are needed to help organize and execute medical studies. Statistical assistance is often needed, for example, in preparing reports on clinical research.

"There have been instances in recent years of international therapeutic 'fads' initiated by publications based on inadequately controlled investigations," Dr. Soffer said.

The medical author, he said, should recognize his need for assistance from these specialist groups.

"Much too frequently in contemporary (medical) literature, methods obscure the goal; those who work almost exclusively with animals require the stimulation of men whose vocation is at the bedside," he said. "Mutual respect and awareness

(Continued on Page 49)

**CALIFORNIA MEDICINE**



## Private Physicians Needed in Research

(Continued from Page 44)

of the potential in both the 'practitioner's camp' and the 'researcher's camp' can result in a sorely required clinical direction in some aspects of institutional research."

### Eye Lens Aging of Radar Workers

Faster-than-average eye lens aging has been found among those who work with high-powered radar equipment.

A report in a recent American Medical Association publication points out, however, that it is impossible at present to relate this effect to vision impairment.

Two investigators from the New York University Medical Center examined 736 persons who worked with microwave equipment at 16 locations. They also examined 559 persons from the same areas who were not exposed to microwave radiation.

They found significantly greater numbers of minor lens defects among the radar workers. The defects were the same types associated with aging of eye lenses, the authors said.

It was determined that certain types of radar work were associated with accelerated lens aging. Those who worked in radar research and development had greater numbers of minor eye defects than radar installers, operators, or maintenance men.

Further statistical studies indicated that it was microwave radiation, not x-radiation from radar-set tubes, which contributed to the lens aging. In fact, workers with the greatest exposure to x-radiation had the lowest incidence of eye defects.

Younger men who had worked with higher-powered equipment were found to have greater numbers of eye changes than some older men who had worked longer periods with lower-powered equipment.

The investigators stress that more research is needed to determine the significance of microwave radiation to lens damage.

"Occupational exposure to microwave radiation may be implicated as a stress which increases the rate of lens aging, although it is impossible at present to relate this effect to functional impairment such as loss of visual acuity or cataracts," the authors said.

Earlier research indicated that cataracts eventually formed on the eyes of rabbits exposed to prolonged microwave radiation, they said.

The report appears in the January *Archives of Environmental Health*, published by the AMA. The authors are S. F. Cleary, Ph.D., and B. S. Pasternack, Ph.D., of the Institute of Environmental Medicine, New York University Medical Center, New York City.



### Openings in General Medicine and Psychiatry in State hospitals and youth and adult correctional facilities

Although most vacancies are in the field of psychiatry, there are frequent openings in general medicine in State facilities. These offer opportunity to develop psychiatric skills if interested.

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## Incident on a Nuclear Submarine

What does the ship's doctor do when the crew of a nuclear submarine is hit by severe respiratory illness?

In one instance, he did what many family physicians would: he ordered his patients to bed, told them to drink plenty of liquids, and administered cough and pain remedies. Most of the men recovered within a few days.

It was an unusual situation, however, which threatened the operating efficiency of the submarine, reports the March 14 *Journal of the American Medical Association*. In some respects, it was an unusual infection, too.

The U.S.S. Sam Houston, a ballistic-missile submarine, was 26 days out on an undersea patrol when the illness began to strike. Because of operational restrictions, the submarine couldn't surface or raise its snorkel for outside air.

The close quarters of the submarine provided an interesting laboratory to study the transmission of the infection, report Lt. Robert Sawyer, M.C., U.S.N., and Robert G. Sommerville, M.D., M.C. Dr. Sawyer was the ship's physician. Dr. Sommerville is on the staff of Belvedere Hospital, Glasgow, Scotland.

Unusual aspects of the incident were that the first case of illness did not develop until 26 days after the submarine began its patrol. The second case developed nine days later. Then the infection spread rapidly, eventually affecting 16 crewmen.

They suffered headache, fever, muscular aches, and a dry cough.

After 10 cases had developed, all nonessential work aboard the submarine was suspended. The outbreak was regarded with "considerable interest and trepidation," the authors said, for it was feared that the submarine's operational readiness would be impaired.

The infectious agent isolated in several of the men was *Mycoplasma pneumoniae*, which is sometimes associated with acute respiratory infections.

*M. pneumoniae* was known to have been present among the population of western Scotland when the crew arrived there to begin its patrol at Holy Loch, the report said. The curious aspect of the infection was that it waited so long—26 days—to develop.

As suddenly as they began, the infections began to level off. The ship returned to normal operation three or four days after the last crewman became ill. It was surprising, the authors said, that more cases did not develop.

The ship continued its eight-week patrol, and all of the sick crew-members had recovered by the time they were taken off on a submarine tender.



### Little-known moments in history No. 1:

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**References:** 1. Based on 1965 data from independent physicians' market survey organization. 2. Seal, J. C.: Eye Ear Nose & Throat Month. 38:738 (Sept.) 1959.



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(Continued from Page 48)

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**GENERAL PRACTICE RESIDENCY**—Approved two-year program; 620-bed county general hospital; Board certified, medical school affiliated, full-time Chief of Medicine; visiting medical school professors weekly; cardiac monitoring coronary care unit; extensive teaching program; outpatient clinic with supervised teaching, all sub-specialties. All intern positions filled 1966-67. Salary: \$400-\$425; plus housing allowance (\$100 single, \$150 married). Contact: B. J. Caldwell, Administrator, Kern County General Hospital, 1830 Flower Street, Bakersfield, California 93305.

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(Continued on Page 56)

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# BOOKS RECEIVED

*Books received by CALIFORNIA MEDICINE are acknowledged in this column. Selections will be made for more extensive review in the interest of readers as space permits.*

**BECK'S OBSTETRICAL PRACTICE**—Eighth Edition—E. Stewart Taylor, M.D., Professor and Chairman, Department of Obstetrics and Gynecology, University of Colorado School of Medicine, Denver, Colorado. The Williams & Wilkins Company, Baltimore, Md., 1966. 658 pages, \$14.50.

**THE CAT: FACTS ABOUT FANTASY**—Mary R. Harworth, Ph.D., Senior Clinical Psychologist, Children's Service, Nebraska Psychiatric Institute; Associate Professor of Medical Psychology, University of Nebraska College of Medicine. With a foreword by Leopold Bellak, M.D. Grune & Stratton, Inc., New York, 1966. 322 pages, \$9.75.

**DISORDERS OF CARBOHYDRATE METABOLISM IN INFANCY**—Marvin Cornblath, M.D., Professor of Pediatrics, The University of Illinois College of Medicine, Chicago; and Robert Schwartz, M.D., Associate Professor of Pediatrics, Western Reserve University School of Medicine; Cleveland Metropolitan General Hospital. Volume III in the Series: Major Problems in Clinical Pediatrics—Alexander J. Schaffer, Consulting Editor. W. B. Saunders Company, Philadelphia and London, 1966. 297 pages, \$8.50.

**FUNDAMENTALS OF CLINICAL HEMATOLOGY**—Second Edition—Byrd S. Leavell, M.D., Professor of Internal Medicine; Physician-in-Charge, Hematology Section, School of Medicine, University of Virginia; Attending Physician, University of Virginia Hospital; and Oscar A. Thorup, Jr., M.D., Associate Professor of Internal Medicine; Physician-in-Charge, Hematology Clinic, School of Medicine, University of Virginia; Attending Physician, University of Virginia Hospital. W. B. Saunders Company, Philadelphia, 1966. 597 pages, \$12.50.

**THE HEART—Its Function in Health and Disease**—Arthur Selzer, M.D. University of California Press, Berkeley and Los Angeles, 1966. 301 pages, \$5.95.

**INJURIES OF NERVES AND THEIR CONSEQUENCES** (Vol. II IN AMERICAN ACADEMY OF NEUROLOGY REPRINT SERIES ISSUED BY DOVER)—S. Weir Mitchell, M.D. With a new Introduction by Lawrence C. McHenry, Jr. Dover Publications, Inc., New York, 1965. 377 pages, \$2.75 (Paperback).

**LUPUS ERYTHEMATOSUS—A Review of the Current Status of Discoid and Systemic Lupus Erythematosus and Their Variants**—edited by Edmund L. Dubois, M.D., Associate Clinical Professor of Medicine, University of Southern California School of Medicine; Director of the "Collagen Disease" Clinic, The Los Angeles County General Hospital, Los Angeles, Calif. McGraw-Hill Book Company (The Blakiston Division), New York, 1966. 479 pages, \$27.50.

**PHARMACOLOGY AND PATIENT CARE**—Second Edition—by Solomon Garb, M.D., Associate Professor of Pharmacology, University of Missouri, School of Medicine; and Betty Jean Crim, R.N., M.Ed.; Assistant Professor of Nursing, University of Missouri, School of Nursing. Springer Publishing Company, Inc., New York, 1966. 469 pages, \$1.75 (flexible cover). (Also available hardbound for \$6.25.)

**WILLIAMS OBSTETRICS**—Thirteenth Edition—Nicholson J. Eastman, Professor Emeritus of Obstetrics, School of Medicine, The Johns Hopkins University; Obstetrician-in-Chief Emeritus to The Johns Hopkins Hospital, Baltimore, Maryland; and Louis M. Hellman, Professor and Chairman, Department of Obstetrics and Gynecology, State University of New York, Downstate Medical Center; Director of Obstetrics and Gynecology, Kings County Hospital, Brooklyn, New York. With the collaboration of Jack A. Pritchard, Professor and Chairman, Department of Obstetrics and Gynecology, Southwestern Medical School; Chief of Obstetrics and Gynecology, Parkland Memorial Hospital, Dallas, Texas; and with the assistance of Ralph M. Wynn, Assistant Professor, Department of Obstetrics and Gynecology, State University of New York, Downstate Medical Center. Appleton-Century-Crofts (Division of Meredith Publishing Company), 34 West 33rd Street, New York, N.Y., 1966. 1182 pages, \$18.75.

**CURRENT THERAPY**—1966—Latest Approved Methods of Treatment for The Practicing Physician. W. B. Saunders Company, Philadelphia and London, 1966. 857 pages, \$13.00.

**MANAGING YOUR CORONARY**—Third Edition—Dr. William A. Brams (Revised). J. B. Lippincott Company, East Washington Square, Philadelphia, Pa., 1966. 175 pages, \$3.75.

**PRINCIPLES OF PATHOLOGY**—Second Edition—Howard C. Hopps, M.D., Chief, Division of Geographic Pathology, The Armed Forces Institute of Pathology. Appleton-Century Crofts, New York, N.Y., 1964. 403 pages, \$8.95.

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1. Wolf, R. L., Mendlowitz, M., Naftchi, N. E., and Gitlow, S. E.: Current Treatment of Hypertension with Drugs, Amer. Heart J. 66:414, Sept., 1963.

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## Perils of Quackery To Be Discussed

Fads and fallacies in the health field will be the subject of the Third National Congress on Medical Quackery, to be held here in October.

From 750 to 1,000 representatives of education, government, professional and voluntary health organizations are expected to attend the meeting October 7-8 at the Pick-Congress Hotel.

It's the first time the meeting will be in Chicago.

Two previous national conferences on quackery were in Washington, D.C.

Joint announcement of the Congress was made by F. J. L. Blasingame, M.D., executive vice-

president of the American Medical Association, and Peter G. Meek, executive director of the National Health Council.

The AMA and the National Health Council, the nation's largest organization of professional, governmental and voluntary agencies in the health field, will be co-sponsors of the Congress.

Details of the program will be announced in the near future. Inquiries should be addressed to John G. Thomsen, M.D., Chairman, American Medical Association Committee on Quackery, 535 N. Dearborn St., Chicago, Illinois 60610.

## Safety in Track and Field

Safety is a major consideration as a million school and college athletes compete in track and field this spring.

The flying javelin, shot put, and discus can be lethal weapons. Even a runner can inflict serious injury to bystanders, fellow athletes and himself on a poorly supervised track.

Good safety supervision is increasingly important at track meets and practice, say the National Federation of State High School Athletic Associations and the American Medical Association's Committee on the Medical Aspects of Sports. In addition to a million varsity competitors, another four million youngsters are participating this spring in intramural track and field. Community recreation programs also are expanding their activities in track and field.

The typical track meet has several events underway at once, sometimes under crowded conditions. Practice sessions pose even more problems because of their informal conduct. The AMA and the National Federation offer these safety suggestions:

—The field area should be laid out so that danger zones of adjacent events do not overlap.

—Competitors should be matched and scheduled by skill level, both for instructional and safety reasons.

—Until he improves his skill, the beginning discus thrower should use a rubber practice discus. He should throw only into a protected area, such as a hanging net or canvas.

—Equipment and track should be examined often.

—Lane restrictions should be enforced during track practice (with eight lanes, the inside two are for runners, the next two for joggers, the next two for walkers, and the outside lanes for hurdlers).

—Beginning hurdlers should practice on grass, with demountable hurdle crossbars.

Many other considerations should be part of a track and field safety plan. Spring practice should begin with a complete medical evaluation of every athlete.

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## Openings in General Medicine and Psychiatry in State hospitals and youth and adult correctional facilities

Although most vacancies are in the field of psychiatry, there are frequent openings in general medicine in State facilities. These offer opportunity to develop psychiatric skills if interested.

Because of the wide variety in medical and rehabilitation activities in both mental health and correctional institutions, many doctors can broaden their experience in State service, and enter for that reason. Your inquiry is invited.

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Volume 37, No. 2  
March-April, 1966

## Health Implications of Fad Reducing Diets

### SUMMARY

Through the years many fad diets have been used for weight reduction. They appeal to obese individuals because they are claimed to offer a quick and easy solution to a difficult problem. Many fad diets have unusual proportions of fat, carbohydrate and protein and may be deficient in one or more nutrients. Adherence to fad diets may endanger health; total fasting is particularly hazardous. The fact that obesity is a complex medical problem and should be treated as such requires emphasis. The importance of physical activity and the influence of psychological factors in weight reduction should be more fully appreciated.

Obesity was recognized as an "affliction" over a hundred years ago as was the fact that weight could be lost "by the most simple common sense means".(1) The question of by what method an obese person should reduce, however, has been the subject of much controversy in the intervening years. Why is weight reduction such a problem? One of the reasons is that food represents many things to human beings in addition to nourishment. Food habits are closely intertwined with the ethnic, religious, and familial culture. Most social functions involve eating; in many cases it is the predominant feature. And eating provides satisfaction and relief from stress which, for some people, can be obtained in no other way.

### OBESITY A COMPLEX PROBLEM

It is becoming increasingly recognized that "obesity is not a disease entity as such but merely a symptom of some underlying difficulty which may have many causes."(2) Genetic, physiologic, psychologic and socioeconomic influences may contribute in

various degrees and interrelationships to the development and perpetuation of obesity. When the complexity of the etiology of obesity is recognized, the unreasonableness of expecting to find a simple cure which will be effective in all cases becomes apparent. Weight reduction and subsequent maintenance of desirable weight requires motivation on the part of the patient, a carefully planned diet which will meet all the nutrient requirements of the individual except for calories, nutrition education to help in establishing new dietary patterns and psychologic support. It takes time and will power.

Desirable weight is basically a matter of balance—correct balance between energy intake and energy expenditure. "Many people have a built-in balancing system that functions without conscious effort. As activity decreases, caloric intake decreases. Others must obtain this balance by consciously limiting intake of food and/or increasing activity."(3) For many people, particularly for the affluent and sedentary, maintaining a balance is very difficult and weight accumulates.



## WHAT ARE FAD DIETS?

Fad reducing diets often are very different from the ordinary diet in their proportions of carbohydrate, fat and protein and may be limited to only a few foods. They are frequently deficient in one or more nutrients. Fad diets are attractive because they are claimed to offer a quick and easy "cure" for obesity. "It is universally tempting to get something for nothing and to avoid facing the effort, frustration, and risks of failure which are essential to realistic success in overcoming or improving the stressful situation." (4) Fad diets are not new; the search for a "magic" cure for obesity has been going on for many years. In 1890 there was a paper in Lancet titled "A Diet of Lean Meat and Water". (5)

Weight may be lost on fad diets, but the reduced weight is seldom maintained. Diets which do not permit an interesting variety of foods usually are not adhered to for long periods of time. Therefore, the individual reverts to his former eating habits and his former weight.

## LOW-PROTEIN DIETS

Restricted dietary regimens have been devised utilizing all possible variations in the proportions of the three energy-yielding nutrients. In many instances, fad reducing diets reflect scientific research. For example, about 10 years ago, two mass-circulation popular magazines published articles on the "Rockefeller Diet". This was based on a low-protein experimental diet (30-40 gm daily) originally described, with relevant data, in reputable scientific journals. (6,7,8) As the Council on Foods and Nutrition of the American Medical Association pointed out, "The experimental character of such an abnormal diet makes it imperative for the physician to recommend its use only after careful investigation. The advocacy of the use of this diet by nonmedical persons is condemned because of its possible harmful effect under certain situations." It was also emphasized that "Obesity is a medical problem and as such should be handled by a physician who will decide whether weight reduction is necessary and safe and, if so, the means by which such reduction should be carried out". (9)

The banana and milk diet is another fad diet

which is inadequate in protein. In a scientific study of this diet, 12 obese women were kept on a daily diet of 1 qt. of skimmed milk and 6 bananas for 6 days. Ten of the subjects were in negative nitrogen balance. Nitrogen loss varied from 0.69 to 3.02 gm a day, representing a loss of 30 to 132 gm protein or 160 to 700 gm protein tissue per week. (10) It was thus demonstrated that 34 gm of milk protein, supplemented by small amounts of banana protein, was inadequate to meet the body needs of these obese women for protein during the first week of weight reduction.

An adequate protein intake is basic for health. Reducing diets, as well as the normal diet, should contain sufficient protein to maintain the body structure.

## LOW-CARBOHYDRATE DIETS

Another group of popular diets for weight reduction is the "eat-all-you-want" type. These have been circulated as the "Drinking Man's Diet", the "Mayo Clinic Diet" and the "Air Force Diet". Disclaimers have been published by the Mayo Clinic (11) and the Air Force. (12) In these diets, carbohydrate intake is reduced to 60 gm or less daily, while fat and protein foods are allowed in any quantity. They are understandably appealing to the obese individual since consumption of fat and protein is unlimited. Such a diet has a high satiety value; weight loss shows up quickly and the dieter is encouraged. (13)

The "scientific basis" given for the effectiveness of low-carbohydrate diets is that carbohydrates are rapidly converted to adipose tissue in the fat person rather than being used for energy. Calories from fat and protein, on the other hand, are burned up in the metabolic processes and are not stored as body fat. (14) Actually, the initial weight reduction on a very low-carbohydrate diet is due to a loss of body water. Continued weight loss on such a diet has been demonstrated to be the result of caloric, not just carbohydrate, restriction. (13)

Carbohydrate is an essential nutrient. The body has a specific need for carbohydrate as a source of energy for the brain and for certain other specialized purposes. The Food and Nutrition Board - National Research Council has suggested that the normal adult



requires approximately 500 carbohydrate calories daily. These must be provided in the diet or derived from protein and fat.(15) Glucose is synthesized from protein only in certain body tissues and at a rate insufficient to meet specific demands. Furthermore, the excretion of the nitrogen from the protein breakdown places an extra work load on the kidney. Carbohydrate is required for fat (either dietary or body fat) to be oxidized in the body. In the absence of a sufficient amount of carbohydrate, an intermediary product of fat metabolism, acetyl CoA, accumulates and condenses to form ketones which accumulate in the blood resulting in ketosis.(14) Since many obese patients have potential or existent renal and cardiac disease, a nonphysiologic burden on these systems by the products of fat and protein catabolism may prove deleterious. Furthermore, the high fat intake is undesirable in terms of possibly promoting or aggravating arteriosclerosis.(16) Low-carbohydrate diets also are likely to be deficient in fiber, vitamin C and minerals.

## FORMULA DIETS

Liquid formula diets have been used by physicians therapeutically and in metabolic research for many years.(17) More recently formula diets have become available to consumers for use in weight reduction. The main advantage of such diets is that they provide exact amounts of nutritionally adequate calories and thus provide a simple rigid regimen which requires no knowledge of foods and food values. Such preparations may be safely used by individuals with just a few pounds to lose or at the beginning of the reducing period. They may also be useful as the exclusive replacement of one meal a day for weight control.(18) However, one of the most important goals in any long-term weight control program is educating the individual with regard to adequate dietary practices. The formula diet provides no opportunity for such education. The monotony of the diet makes it unacceptable to most persons for long-term use. Formula diets, although nutritionally adequate, provide no bulk and constipation may become a problem.(19) When the formula diet is abandoned and the individual returns to his former dietary regime, he quickly reverts to his original obese weight.(17)

## FASTING

Total fasting is being used by some physicians as a method of weight reduction in grossly obese patients who have not responded to other methods of treatment. Patients are hospitalized, examined, and metabolic responses to fasting are carefully and regularly evaluated. Fasting should be undertaken only in the hospital under the close supervision of a physician. Unfortunately, the publicity given this procedure in the public press may induce some obese persons to try total fasting without medical supervision. The dangers inherent in total fasting when persons are ambulatory, driving cars and engaging in normal physical activity should also be publicized. There are serious risks involved in fasting individuals when infection, diabetes, liver disease, recent myocardial infarction, peptic ulcer or pregnancy is present.(20) Drenick et al have studied obese patients starved from 12-117 days. Complications which developed were severe orthostatic hypotension, severe normocytic, normochromic anemia and gouty arthritis. These effects were reversed with refeeding. Serum uric acid increased; blood glucose levels fell in some cases. Considerable amounts of body protein and potassium were lost.(21) Even on short-term total fasts (3-10 days) a rise in plasma uric acid and a fall in urinary excretion of uric acid have been consistently demonstrated.(22) "These complications make it imperative that all starvation regimens be carried out with continuous clinical supervision and adequate laboratory analyses."(23)

The ideal weight-reducing program for obesity should produce significant loss of adipose tissue without catabolism of lean tissue. Benoit et al conducted nitrogen balance studies on 7 obese men during 10 days of fasting and reported that 65% of the weight lost during fasting was due to loss of lean body tissue, and only 35% due to loss of adipose tissue. "These results suggest that although clinically desirable weight reduction occurs during fasting, it is at the expense of lean tissue, which is physiologically undesirable."(24)

It has been demonstrated that when weight losses result from the catabolism of lean tissue rather than fat, weight gain is apt to be rapid when adequate intake of protein and calories is resumed. Wishnofsky states:



"After the desired weight loss has been established and the patient placed on a diet adequate to maintain caloric equilibrium, the protein stores which have been depleted during the period of negative balance will be replenished. For every pound of protein replenished, there will be an increase of four pounds in body weight. Thus, even though the patient is in caloric equilibrium, he will continue to gain weight until the protein stores have been completely restored." (25)

## EXERCISE

Obese individuals attempting weight reduction often do not appreciate the important role physical activity may play in the achievement of their goal, or that inactivity may have been a factor in the development of their obesity. Studies in which the activity of obese and nonobese men and women was actually measured revealed that the obese women were far less active than the non-obese control subjects. While obese men were less active than the nonobese men, the difference was not as great as among the women. (26) The degree of participation of obese adolescent boys in active exercises has been found to be generally less than that of nonobese boys. (27) Similarly, obese adolescent girls have been observed to be sig-

nificantly less active than nonobese girls. (28) Buskirk et al found that daily walking clearly contributed to body weight loss in obese subjects on calorie-restricted diets. (29)

## PREVENTION

Certainly in the case of obesity, an ounce of prevention is worth a pound of cure. Follow-up studies of patients who have reduced their weight show that on a long-term basis, treatment of obesity is not very successful. Mayer suggests that "This may be in part because obesity sets up a psychologic chain of events which tends to make the condition self-perpetuating; i.e., obsessive concern with weight leads to passivity, expectation of rejection, greater inactivity, etc. Recent work from my laboratory also suggests that when a subject has once been obese some irreversible physiologic changes occur which may make the regaining of lost weight more 'efficient' than the first weight gain." (30)

Basic habits of food intake and physical activity are established early in childhood and are notably resistant to change. This fact, along with the knowledge that obesity has genetic aspects, indicates the importance of establishing good food and exercise habits in children.

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## BOOKS RECEIVED

Books received by CALIFORNIA MEDICINE are acknowledged in this column. Selections will be made for more extensive review in the interest of readers as space permits.

**CARING FOR THE AGED**—Bertram B. Moss, M.D., with Fraser Kent. Doubleday & Company, Inc., New York, 1966. 372 pages, \$4.95.

**COMPENDIUM OF EMERGENCIES**—Second Edition—Edited by H. Gardiner-Hill, M.D., F.R.C.P., Consultant Physician to St. Thomas's Hospital, London. Butterworth Inc., Washington, D. C., 1965. 374 pages, \$12.00.

**ELECTROCARDIOGRAPHY IN INFANTS AND CHILDREN**—A Symposium Sponsored by The American College of Chest Physicians—Donald E. Cassels, M.D., Professor, Department of Pediatrics, University of Chicago, Illinois; and Robert F. Ziegler, M.D., Physician-in-Charge, Division of Pediatric Cardiology, Henry Ford Hospital, Detroit, Michigan, Editors. Grune & Stratton, Inc., New York, 1966. 366 pages, \$16.75.

**HOSPITAL POLICY DECISIONS: PROCESS AND ACTION**—Arthur B. Moss; Wayne G. Broehl, Jr.; Robert H. Guest; and John W. Hennessey, Jr. Foreword by John R. McGibony, M.D. G. P. Putnam's Sons, New York, 1966. 332 pages, \$8.50.

**MEDICAL CARE OF THE ADOLESCENT**—Second Edition—J. Roswell Gallagher, M.D., Chief, The Adolescents' Unit, Children's Hospital Medical Center; Clinical Professor of Pediatrics, Harvard Medical School, Boston; with eight contributing authors, and The Staff Physicians of the Adolescents' Unit, Appleton-Century-Crofts (Division of Meredith Publishing Company), New York, 1966. 489 pages, \$12.00.

**PATHOLOGY OF THE AGED**—Florence McKeown, M.D., F. C. Path., Reader in Pathology, Queen's University, Belfast; Consultant to the Royal Victoria Hospital, and City Hospital, Belfast. Butterworths, London, 1965. 361 pages, \$15.50.

**PREIMPLANTATION STAGES OF PREGNANCY**—Ciba Foundation Symposium—Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol. and Maeve O'Connor, B.A. Little, Brown and Company, Boston, Mass. 1965. 430 pages, \$13.50.

**PREVENTIVE MEDICINE FOR THE DOCTOR IN HIS COMMUNITY**—Third Edition—An Epidemiologic Approach—Hugh Rodman Leavell, M.D., Dr.P.H., Professor Emeritus of Public Health Practice, Harvard School of Public Health; Consultant on Health, Ford Foundation (India); and E. Gurney Clark, M.D., Dr.P.H., Professor of Epidemiology, School of Public Health and Administrative Medicine of the Faculty of Medicine, Columbia University; and twenty-three contributors. McGraw-Hill Book Company (The Blakiston Division), New York, 1965. 684 pages, \$12.50.

**PSYCHOPATHOLOGY OF SCHIZOPHRENIA**—The Proceedings of the Fifty-Fourth Annual Meeting of the American Psychopathological Association, Held in New York City, February 1964—Edited by Paul H. Hoch, M.D., Department of Mental Hygiene, State of New York; College of Physicians and Surgeons, Columbia University, New York City; and Joseph Zubin, Ph.D., Department of Mental Hygiene, State of New York; Department of Psychology, Columbia University, New York City.

**TODAY'S HOSPITAL**—A Guide for Trustees, Administrators, and Volunteers—Raymond P. Sloan. Harper & Row, Publishers, Inc., New York, 1966. 212 pages, \$4.50.

**TRANSCULTURAL PSYCHIATRY**—Ciba Foundation Symposium—Edited by A. V. S. De Reuck, M.Sc., D.I.C., A.R.C.S., and Ruth Porter, M.R.C.P. Little, Brown and Company, Boston, Mass. 1965. 396 pages, \$12.00.

**VECTORS OF DISEASES OF NATURAL FOCI**—P. A. Petrishcheva, Editor. Translated from Russian by B. Hershkovitz, M.Sc. Translation edited by Prof. O. Theodor. Israel Program for Scientific Translations, Jerusalem 1965. Published in the U.S.A. by: Daniel Davey & Co., Inc., 257 Park Avenue South, New York, N.Y., 1966. 332 pages, \$12.75.

**YOUR ULCER: PREVENTION, CONTROL, CURE**—G. S. Serino, M.D., M.Sc. (Surg.), F.I.C.S. Illustrated by Lois Carl Fargo. J. B. Lippincott Company, Philadelphia and New York, 1966. 162 pages, \$3.50.

## REFERENCES AND REVIEWS

**ALDOSE CARRIERS IN HUMAN ERYTHROCYTES**—P. Bican and L. Lacko (U. nemocnice 1, Prague, Czechoslovakia). Transfusion, 6:130-133 (March-April) 1966.

Galactose, having the common carrier system of aldoses, enters erythrocytes from the medium in exchange for glucose and temporarily reaches higher levels (apparent steady state) than its concentration in the medium. The apparent steady states in fresh and stored human erythrocytes of donors of a certain age range were studied. Decreased values of galactose in the apparent steady state were observed in erythrocytes after 14 days of storage.

\* \* \*

**COMPARISON OF THE ACID-BASE BALANCE IN CISTERNAL AND LUMBAR CEREBROSPINAL FLUID**—A. N. P. van Heijst (State University Hosp., Utrecht, Netherlands). A. H. J. Maas and B. J. Visser. Pflueger Arch. Ges. Physiol., 247:242-246 (No. 3), 1966.

Although the arterial blood showed no indication of respiratory or metabolic changes, the mean pH value of cisternal cerebrospinal fluid was found to be 0.021 pH units higher, and the mean PCO<sub>2</sub> was 2.53 mm Hg lower than the corresponding values in simultaneously sampled lumbar cerebrospinal fluid.

(Continued on Page 33)

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## NEW BOOK

**FUNDAMENTALS OF INTERNAL MEDICINE.** By Robert P. McCombs, M.D., 3rd ed., 845 pages. 1965. Year Book, \$13. A new edition of this popular book will be warmly welcomed. Originally intended to meet the need for a "short" book on the practice of medicine, it is compact, concise, moderately priced, and thoroughly utilitarian. Genetic defects, infections, hypersensitivity reactions, metabolic disorders, and cardiovascular, pulmonary, renal, endocrine, gastrointestinal, hematological and musculoskeletal diseases are all here.

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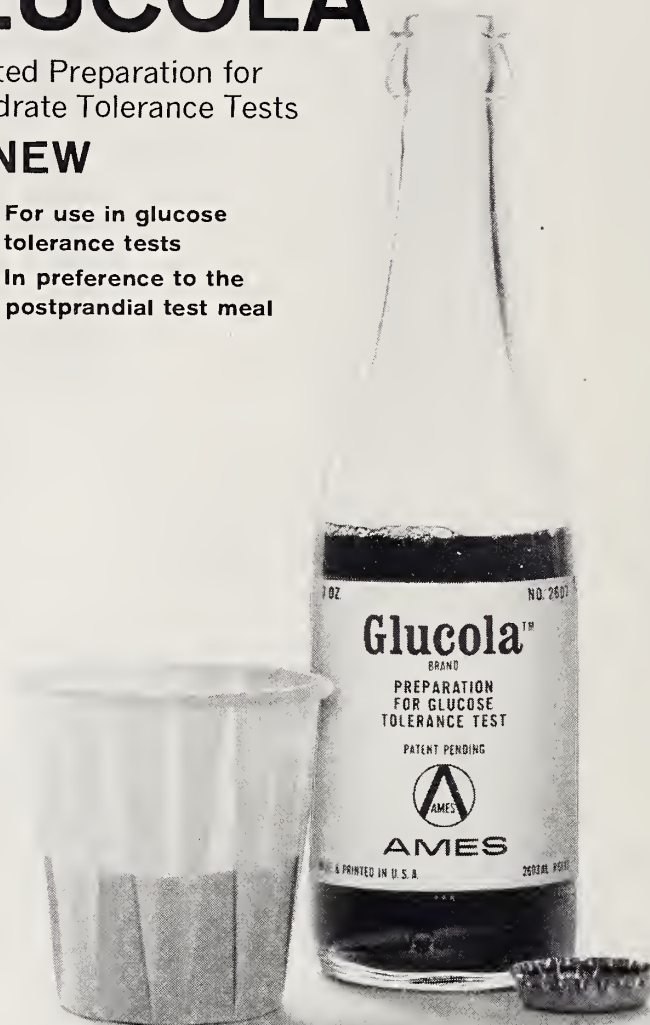
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## Mental Resistance To Influenza

Some of us may have mental resistance which helps fight off the flu after infection, while others become ill because they are psychologically vulnerable.

This is indicated by research reported in a recent American Medical Association publication.

There is even a suggestion—although the statistical evidence is not strong—that mental make-up helps prevent the infection itself.

When physicians tested 480 men employees at the Army Biological Laboratories, Fort Detrick, M.D., they found 96 who could be classed as "psychologically vulnerable" to illness, and another 78 who were termed "intermediates."

The remaining 306 were "nonvulnerable," a term indicating a relationship between their psychological health, as determined by testing, and their speed of convalescence from previous illness.

When an outbreak of Asian influenza struck the installation the "vulnerable" men reported illness almost 2½ times as frequently as the nonvulnerable.

In both groups, only one in every six men infected by flu virus actually became ill. There was a slightly larger percentage of infection, however, among the vulnerable.

The differences between these infection rates were not statistically significant, but they are "suggestive" of an increased rate of infection in psychologically vulnerable persons, the authors said.

Flu vaccinations proved ineffective in this instance, and did not affect results of the survey. Infection rates were the same among vaccinated and unvaccinated men.

The authors point out that the men at Fort Detrick were particularly suited for this type of study. They were of approximately the same age, and had a high level of education.

They also had a good reason to report any illness: the military laboratory works with many kinds of pathogenic microorganisms. The men had orders to report immediately if they felt ill.

In addition, all of the men had undergone psychological testing before the influenza epidemic. Thus, there was little danger that illness influenced their test ratings.

Authors of the report are Leighton E. Cluff, M.D., and John B. Imboden, of the Johns Hopkins University School of Medicine, Baltimore, and Arthur Canter, M.D., of the College of Medicine, University of Iowa, Iowa City.

The report appeared in the February issue of the *Archives of Internal Medicine*, published by the AMA.



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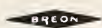
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## Hechter, Godall Appointed To Biomedical Institute

Two scientists were named recently to the Institute for Biomedical Research of the American Medical Association Education and Research Foundation.

They are Oscar Hechter, Ph.D., for the past 21 years a Senior Scientist at the Worcester Foundation for Experimental Biology, Shrewsbury, Mass., and M. C. Goodall, Research Associate in the Physics Department at Boston University.

The appointments were announced by Raymond M. McKeown, M.D., President of the AMA-ERF.

Dr. Hechter, who was appointed a member of the Institute, is an authority on the chemical structure and functions of hormones. He currently is investigating the mechanisms by which information carried by hormone molecules is transferred between the living cell and its environment as well as between the functional parts of cells.

In 1950 he received the Ciba Award from the Endocrine Society for his pioneering studies of how certain steroid hormones are formed from cholesterol by a portion of the adrenal gland. This work, which stimulated a wide range of further research into hormones, had important implications for steroid hormone production by the pharmaceutical industry.

While at the Worcester Foundation, Dr. Hechter also served as Research Professor of Physiology and Biology at Boston University (1951-1958), and Visiting Professor of Biology at Brandeis University (1961-1962). Previously he was a research associate in the Department of Metabolism and Endocrinology, Michael Reese Hospital, Chicago (1937-1940) and at Cedars of Lebanon Hospital, Los Angeles (1940-1944).

Born in Chicago in 1916, Dr. Hechter graduated from the University of Chicago in 1938 and received a Ph.D. in biochemistry from the University of Southern California in 1943. He is a Fellow of the American Academy of Arts and Sciences and a number of professional societies.

Dr. Hechter is married and has one son. His wife, Gertrude, is a painter and graphic artist, who has exhibited widely in the East.

Goodall, an associate member, will work with Dr. Hechter. Along with experiments in electronics, he has investigated energy systems involved in muscular contractions and higher through processes by the brain.

An honors student at Oxford University, England, Goodall was experimental officer in microwave radar at the Admiralty Signals Establishment at Bristol, England during World War II.

He became a member of the Institute for Advanced Study, Princeton, N.J. in 1949 and later

(Continued on Page 36)



## REFERENCES AND REVIEWS

(Continued from Page 17)

**PATHOGENESIS OF INTRAMYOCARDIAL EPITHELIAL INCLUSION CYSTS**—K. W. Lanks and E. V. Lautsch (Broad and Ontario streets, Philadelphia). *Arch. Path.*, 81: 365-367 (April) 1966.

Two types of intracardiac epithelial heterotopia are discussed on the basis of morphology, location, and clinical findings. One type, a cystic lesion, is considered to be a fragment of the esophageal primordium which has undergone differentiation in an ectopic position. The pathogenesis of a second, equally uncommon, glandular variety is also discussed. These lesions may represent foregut fragments developing in a different environment, or they may very well be true neoplasms of endothelial or mesothelial origin.

\* \* \*

**PUPILLARY REACTIVITY, PSYCHOLOGICAL DISORDER, AND AGE**—A. McCawley (400 Washington St., Hartford, Conn.). C. F. Stroebel and B. C. Glueck, Jr. *Arch. Gen. Psychiat.*, 14:415-418 (April) 1966.

The rates of pupillary dilation (adrenergic index) and constriction (cholinergic index) in 94 normal control subjects were used to evaluate the autonomic nervous system balance of 47 psychiatric inpatients. When the control and patient groups were matched by decade of age, the patient group showed greater variability in pupillary reactivity but not sufficient for classification purposes. Variability of both constriction and dilatation in the control group was observed to be a monotonically increasing function of age.

\* \* \*

**A CONCEPTUAL MODEL OF SLEEP**—K. Gaardner (National Institute of Mental Health, St. Elizabeth's Hosp., Washington, D.C.). *Arch. Gen. Psychiat.*, 14:253 (March) 1966.

A general systems' model of sleep is presented, using analogy to general purpose digital computers. It is proposed that the two main functions of sleep are to destructure or erase data storage and to reinforce the program (character) of the organism. Single-cell studies and other recent research are interpreted as supporting the model. The model is used to reconcile observations of changed sensory input, changed sleep need, character patterns, and brain changes.

\* \* \*

**SIMPLE MAIL-IN METHOD FOR CHROMOSOME ANALYSIS**—T. R. Birdwell, R. R. Eggen, and R. M. Dimmette (U.S. Naval Hosp., San Diego, Calif.). *Amer. J. Clin. Path.*, 45:153 (Feb.) 1966.

A simplified method for mailing human blood for chromosome analysis is described. Rather than using tissue culture medium and/or complex methods of temperature control, the samples are mailed in sterile, heparinized, containers and are cultured after their arrival at the reference laboratory. Successful cultures were obtained from samples sent from as far away as 7,000 miles (Cairo, Egypt).

\* \* \*

**MARKED AORTIC REGURGITATION WITHOUT PERIPHERAL VASCULAR SIGNS**—M. A. Demony and H. A. Zimmerman (250 Hanna Bldg., Cleveland). *Dis. Chest*, 1:61 (Jan.) 1966.

Seven patients with marked aortic regurgitation proved by cineangiography are reported, but without the usual peripheral vascular phenomena which are low diastolic and high pulse pressure, Corrigan pulse, visible arterial pulsations (Corrigan's sign), pistol shot sound over the femoral artery, Duroziez's sign, Traube's sign and capillary pulse.

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## The Medical Practitioner, Alcoholism And Motivation

MAX HAYMAN, M.D., *Los Angeles*

■ *Adverse influences on motivation for recovery from alcoholism must be searched for in three areas: society, the medical practitioner and the patient. Society is ambivalent because there is a vicarious release through identification with the cheerful "drunk" coupled with unconscious envy and resentment leading to punitive action.*

*The current "alcohol culture" decrees that to drink is to be well, not to drink is to be ill.*

*The medical profession attempts to suppress, deny, rationalize or reject the problem of alcoholism because it involves a change in attitude and recognition of limitations.*

*The alcoholic patient has a notorious lack of motivation, but this must be recognized as a symptom of his disease, and with certain techniques this symptom is treatable. Furthermore, motivation fluctuates and many opportunities for treatment are available when the medical practitioner can detect that motivation is high. At times a coercive approach is required, at times a permissive one; and the optimal use of such approaches will increase the motivation to an effective level.*

THERE IS MUCH ambivalence in society's attitude toward the alcoholic. For example, drunkenness can be considered as humorous, as a jailable offense or as an extenuating circumstance in such crimes as murder.

The motivations that lead to society's ambiva-

lence appear to be based partly upon a vicarious experience of expansiveness and release of inhibitions through identification with the cheerful drunk, and an often unconscious envy and resentment. When the alcoholic passes the tenuous borderline of "good taste," the good humor may change into overt resentment, and society may institute severe repressive measures. Because of guilt in gratification of "forbidden" impulses through the alcoholic, there is a subsequent need for punitive action against him, and he becomes the scapegoat.

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Some of the data in this paper will be included in a forthcoming volume, "Alcoholism: Mechanism and Management" to be published by Charles C Thomas, Springfield, Illinois.

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Many of the contradictory measures in connection with the licensing of establishments for the sale of alcoholic beverages, the use of tax imposts, and the talk, if not action, of control of advertising of alcoholic beverages, are witness to society's fluctuating attitudes. The denial, suppression and confusion of the problem of alcoholism by the community are paralleled by the deliberations of the Food and Drug Administration and other governmental organizations concerning the labeling of cigarettes as a toxic substance. Alcohol has been known for hundreds of years to be toxic, yet not much attention has been given to suggestions (such as Myerson's<sup>23</sup>) that liquor be labeled as a habit-forming, noxious substance.

### **The Alcohol Culture**

Despite praise of alcohol in a recent symposium,<sup>19</sup> and in a recent book,<sup>4</sup> it is not a physiological need of the human organism. It seems a rationalization that the pace of civilization demands the use of alcohol, when there may be evidence that even social drinking may increase mortality. Oddly, the diner who refuses to drink is often looked at askance, whereas an explanation that he is a member of Alcoholics Anonymous is followed by immediate understanding. Apparently to drink is to be well, not to drink is to be ill.<sup>4</sup> When a large majority of adults drink, it is taken for granted that sobriety is abnormality. To avoid such a brand, adults and teenagers may be motivated to drink in spite of other factors influencing them to abstinence.

### **The Change in Cultural Attitude to Alcohol**

It is often said that the prevention of alcoholism, depending as it does on cultural attitudes, is an impossible area to attack. Fortunately, however, this has not been discouraging to everyone and active research is going on in this important field.<sup>10,17</sup> The recognition of the early signs of alcoholism as a significant indication of maladjustment, consistent social disapproval of excessive drinking, and, eventually, the teaching of young children—pre-school and grammar-school age—that alcohol is not a legitimate method of handling emotional problems should considerably ameliorate the problem. Such early training would, of course, require a society-approved consensus regarding "normal" and deviant drinking habits. The more ambivalent the cultural and parental atti-

tudes, the more unpredictable the attitude of the young.

### **Motivation in the Medical Profession**

In our 1956 survey, it was demonstrated that persons addicted to alcohol, although recognized as a legitimate focus of interest by medical practitioners, were generally either rejected or only occasionally accepted for treatment.<sup>11</sup> When treatment was attempted, the results were notoriously poor. Therefore, leadership in the fields of prevention and treatment of alcoholism has fallen to social workers, psychologists, educators, Alcoholics Anonymous, and, more recently, public health officers.

### **Rationalizations of Physicians**

The caring professions, however, just as society as a whole, have attempted to suppress, deny, rationalize or ignore the problem. Alcoholics, they say, for example, are incurable, or they represent a moral problem, not one of disease, or they don't want to get well, or there is no time to treat them adequately. Only the most intrepid souls seem willing to accept the challenge of alcoholism and often the accompanying opprobrium and downgrading. Perhaps those who have less need to be omnipotent and to cure all their patients, or less need to have dutiful patients, or even those who have, in a reverse way, masochistic needs, will treat alcoholics. In any event, defective techniques, inadequate case finding and incomplete medical histories noted in a recent study indicate the discomfort of the medical practitioner and his disinclination to treat alcoholics.<sup>16</sup>

### **The Antidote**

The cure for such rationalizations has become apparent. It includes increased motivation, information, education and training. Supervision of medical practitioners' treatment of alcoholics reveals that problems of motivation often supersede deficiencies in knowledge and technique. Attitudes of hopelessness toward alcoholics lead to attitudes of helplessness. When the motivations of alcoholics are understood and accepted, physicians can overcome a disinclination to treat them.

### **Motivation in the Patient**

In dealing with an alcoholic, we are almost invariably faced with poor motivation for change. Lack of motivation is so important and is so in-



trinsic to the disorder that it can be considered an integral symptom of the problem drinker. The influence that this lack of motivation has on the attitude of the medical practitioner is well exemplified in a recent survey of state hospital attitudes.<sup>21</sup> Seventy-three per cent of the hospitals reporting indicated that the poor results they reported were due to the poor motivation of the patient.

#### **Types of Motivation**

Anyone dealing with an alcoholic must learn to stimulate the patient's interest in making a change. In this connection, as an analogy, we can look at the two principal methods of pedagogy: the aggressive, forceful and punitive (such as jailing or withdrawal of moral support); and its opposite, the permissive, noncensorious, affectionate and approving, which connotes, essentially, the giving of love and support.<sup>6,7</sup> Both of these general methods can be used—singly, alternately or simultaneously in various admixtures. The situation may demand permissiveness in one area and coercion in another, and the medical practitioner can become quite comfortable with apparently inconsistent attitudes.

We must consider the motivation of the alcoholic for therapy in general and for psychotherapy specifically. The alcoholic is willing to accept hospitalization and drugs in the acute phase. When he is physically and emotionally depleted from his binge or is in a coma, he has no resistance to physical treatment. At such a time he has an immediate need to quell the disturbed and painful physiological sensations, especially during the withdrawal stage. He is well motivated for the physical treatment of the medical practitioner, in which he is a passive participant, but is usually less accessible to psychological treatment, which makes considerable demands upon him. This tendency is even more pronounced in the lower socioeconomic groups,<sup>15</sup> although with alcoholics it is also strong in the higher socioeconomic groups, because of such defense mechanisms as denial or suppression of the problem.

#### **The Basis of Motivation**

What can treatment give to the alcoholic, and what does it take away from him? In the interval between acute withdrawal episodes, deprivation of alcohol is taking from the alcoholic all that makes life worth living. What can he be offered that is

as good? This is something that is frequently difficult to find. Many an alcoholic would find life arduous and unrewarding even without the handicap of alcoholism. Ordinarily, telling the patient that life is good is useless. He has tried to convince himself of this, and many others have undoubtedly told him so for many years. Demonstrating that life is worthwhile does have value, particularly through organizations such as Alcoholics Anonymous, where the patient may participate passively for many weeks, observing that others in a similar situation have begun to regard life as worthwhile.

Most important, of course, is the *experience* that life can be rewarding. Attaining this experience depends primarily on what factors in life the patient considers particularly important, and what he feels the opportunities are for obtaining gratification. These factors are often unconscious, and therefore not accessible to the patient. They may remain unconscious, yet be gratified, as they often are, in the experiences that come with the acceptance of and the carrying out of the principles of Alcoholics Anonymous. The most valuable method of demonstration in the area of medical practice lies in the process of psychotherapy. In such a situation, in a mutual participation and through recognition of misinterpreted experiences, there can be an alteration in attitudes that induces the alcoholic to try again, and, perhaps this time, to recognize and savor some of the "better things in life." It is the patient himself who interprets what these better things are, and when he reaches this point he will be motivated.

#### **Fluctuations in Motivation**

There are many different sources of the motivation that leads an alcoholic to treatment. The recognition that he is ill may fluctuate, coming only at certain times and under certain circumstances and stresses, but advantage should be taken of this reality-orientation, episodic and uncertain as it may be, even if such motivation may actually depend upon secondary gains. For example, it may serve to take pressure off the patient, who can then say, perhaps to a no-longer-tolerant employer or spouse, "You see, I am trying my best to cure myself."

On the other hand, motivation may be diminished by an inadequate external environment from which the patient sees no possibility of escaping, such as an aggressive and domineering mother who

nevertheless cares for and supports him, so that he feels he cannot change his milieu. Or he may have a crippling physical illness which cannot be cured, or some unsightly personal characteristic. Also, much alcoholism is in lower socioeconomic groups where the alcoholic is often of deteriorated or subnormal mentality and would have, at best, little to look forward to. Improvement in social and economic conditions and greater opportunities in life could give many alcoholics the incentive to change their mode of life.

During psychotherapy, motivation may be increased temporarily when the patient ascribes omnipotence to the therapist and has the expectation of magical help. While such illusions may be helpful in the early phase of treatment, this motivation may be quickly dissipated as soon as the patient recognizes reality or becomes disillusioned in the projected powers of the therapist. Alternations in fantasies of the patient may produce alternations in attitudes toward treatment. If the therapist appears as an agent of society, there is often considerable rebellion and hostility, possibly leading to termination of treatment. As long as the patient receives transference gratifications of an infantile nature from the therapist, treatment may progress, and such gratification can be knowingly and systematically given. The patient, through intuitive perception, however, may recognize an unconscious hostile countertransference on the part of the therapist; and, should this occur, there is a rapid decrease in motivation and dissolution of treatment. The very realization by the patient that, to succeed, he must undergo a certain amount of suffering may decrease motivation to the point where therapy is sacrificed.<sup>24</sup>

It should be reemphasized that lack of motivation may be temporary—since this factor does waver and fluctuate—and therefore should not be considered a bar to successful aid. While the alcoholic's defenses are formidable, they are not impregnable.

#### Physicians' Misconceptions of Motivation

Patients with apparently good motivation are more likely to be selected for treatment by medical practitioners and to be helped by psychotherapy.<sup>2</sup> Patients with a psychoneurotic label who are co-operative are more likely to receive help than the sociopath who acts out his impulses and feelings, or the alcoholic who reacts with self-destructive patterns. Yet observation indicates that, even if

the alcoholic is accepted for treatment, there is often so great a countertransference from the therapist that adequate therapy is impossible. A study from the Alcoholism Research Clinic indicates that the patient's compliance with the requirements of psychotherapy, such as attendance, responsiveness and verbalization, was often adopted by the therapist as the chief criterion of motivation for cure.<sup>9</sup> The method may have to be adapted to the case, and rigid attitudes toward the patient's apparent noncooperation may have to be replaced by more permissive ones. Another study has shown that where both motivation in the patient and empathy in the therapist are high, therapy is short and successful. When both are low, therapy is short but unsuccessful. When the therapist's empathy is high but the patient's motivation is low, therapy is long and unsuccessful. Further, experienced therapists tend to view patients as more like themselves, thus reducing psychological distance, whereas inexperienced therapists do the reverse.<sup>3</sup>

#### Inducing Motivation

It is often stated that nothing can be done for the alcoholic until he "hits bottom," at which point his precarious state induces adequate motivation. This is especially emphasized by Alcoholics Anonymous. The phrase "hitting bottom" is understood to mean that the alcoholic has reached his lowest point in deterioration or degradation. He may remain at this point indefinitely, or he may start a slow and tortuous climb. This bottom varies with the individual; it may be at the point of blackouts and physical symptoms, loss of a job, loss of family and friends, or loss of faith in his own abilities. He may even descend to the skid-row level. The medical practitioner, however, through training and tradition, feels obligated to treat the patient at the level at which he presents himself in the office, whether or not he has yet hit bottom. Accordingly, it is especially necessary to be able to inspire motivation in the patient even at this earlier stage.

#### Management of Motivation

Inducing motivation is not always easy, but certain procedures can be useful. For example, the removal of secondary gains may help the patient hit his own particular bottom. Often a wife or mother sympathizes too intensely with the alcoholic, makes excuses for him, calls his employer with the plea of sickness and takes many of the



ordinary responsibilities of living from his shoulders. If the medical practitioner can manage to have these secondary gains withdrawn, it may impel the alcoholic to seek help.<sup>12</sup> The practitioner can also create or precipitate the motivating crisis in other ways. If the patient prizes a special attribute or ability, such as intelligence, it may be possible to precipitate him into treatment by demonstrating an impairment, using psychological tests. In the case of one patient who particularly emphasized his bodily integrity, evidence of liver disorder was the key to motivation for therapy. In another case, it was fear of insanity. Or the danger of losing cherished children may lead to "surrender" and eventual change, as may delirium tremens, or the decision of a wife to leave her alcoholic husband. For example:

The husband of a patient was an alcoholic, but did not acknowledge it. As the wife progressed in therapy she gave up her masochistic attitude toward her husband, attended several Alanon meetings and withdrew her neurotic support of the "alcoholic equilibrium." Shortly thereafter the husband began to read articles on alcoholism. Finally he took one of the tests appearing in a current magazine and decided that he was, indeed, an alcoholic. He joined Alcoholics Anonymous and is still an active member after five years.

Motivation by coercion is thus also important. We can include in this category any reward or punishment important enough to cause the alcoholic to forego the pleasure and needs of drinking, such as the threat of jail, of loss of financial support, or of a job.<sup>18</sup> In the survey mentioned previously, 60 per cent of psychiatrists queried felt that legal commitment of alcoholics to state hospitals was beneficial to treatment. Recovery and improvement rates in industrial clinics where there is considerable coercion are much higher than elsewhere, since the alcoholic is still in a state where his job is of considerable and perhaps overriding importance to him. Few, if any, alcoholics decide to stop drinking until some pressure is put on them,<sup>18</sup> and protecting the patient from the consequences of alcoholism can only postpone treatment and reduce its effectiveness.

#### **The Physician's Role**

At various times the alcoholic may look upon the medical practitioner as a guide, friend, protector or teacher. He may need the practitioner to intervene between his parents and himself or his

wife and himself, or to help with some legal, social or financial problem. The practitioner must have the capacity to understand these needs either by intuitive perception or by the more arduous method of careful history-taking and discussion. When he is alert to these needs, he can fill the role the patient assigns him, thereby relieving anxiety and increasing motivation. The physician must decide whether to accede to such needs or not, depending on the situation at the moment.

Whether or not the fact is consciously recognized, persons who have the most severe type of alcoholism have lost much of the meaning of social interaction and have given up the social mores of the group. Idealism has become ridiculous to them, cultural mores have come to be regarded with destructive cynicism, and problems of life have been met with concealed resentment and outward passivity. Reward and punishment no longer influence them and finally apathy supervenes.<sup>1</sup> Many alcoholics are able to renew previous attitudes toward prevailing mores, but it should be accepted by the physician that many no longer have the capacity to compete in their original milieu and must therefore accept a different job, a different socioeconomic status and different activities from those of their earlier years.

The medical practitioner must also consider removing the alcoholic from his current environment. A vicious circle of drinking, quarreling and further retaliatory drinking may have been established which can be broken only by a temporary removal of the more overtly disruptive member. This is often made easier by a willingness on the part of the alcoholic to trust himself to strangers rather than to a spouse or sober relatives or friends. This can be at least a temporary advantage, can increase motivation and can provide a rationale for hospital care, a foster home or a half-way house.

The physician should be particularly aware of the defense mechanism of denial.<sup>13,22</sup> Its intensity makes it possible for the alcoholic to deny not only the desire for drinking, but also the intense effects, such as anxiety and depression. Frequently when writers speak of anxiety, guilt and depression, they are speaking not of an overt and conscious effect but of an unconscious one. Most often the alcoholic who is sober does not consciously perceive these, although he may claim to. It is only at certain critical times, when a particularly sensitive area is touched, such as

noted above—when a period of depression supervenes, a bad hangover occurs or a confrontation is made which the patient cannot escape—that the denial mechanism breaks down. At these times the alcoholic becomes most accessible to intervention, and such opportunities should be awaited and utilized.

#### The Use of Coercion in Motivation

Other observers have emphasized the need to reinforce abstinence. In one study it was noted that, to the alcoholic, the need for disulfiram or for psychotherapy decreases as the time since the last drinking bout increases. From this observation it was suggested that, for sustained abstinence, pain must be continuously linked with drinking, since the aversive response becomes extinguished. A treatment program, therefore, must provide some method to reinforce the need for abstinence. An important development in the past decade has been the court referral of alcoholics to various helping or treatment modalities. The alcoholics who do best under this coercion have adequate ego strength, higher levels of anxiety and shame, greater response to authority and conscience and more willingness to accept help.<sup>20</sup> Davis and Dittman of the Alcoholism Research Clinic found that over a 15-week period clinic attendance by court-referred patients could equal that of self-referred patients. They concluded that alcoholic outpatients may be as motivated for treatment as nonalcoholic psychiatric patients.<sup>8</sup>

Many workers emphasize a liaison between probation officers and the medical practitioner to aid in maintaining a continuation of therapy. It is of considerable interest that an alcoholic will accept the authority of the judge and faithfully attend the alcoholism clinic or Alcoholics Anonymous when, in actuality, he usually has no abhorrence of jail sentence. Frequently enough such a patient has been jailed many times before. I believe this willingness to obey a court order is due primarily to a projection of paternal or maternal omnipotence onto the figure on the bench and not to the actual temporal power of this authority.

Other nations have attacked the problem of motivation in a similar way. In Czechoslovakia an arrest for drunkenness obliges the individual to attend six lectures on alcoholism.<sup>5</sup> If the person is a chronic alcoholic or has a second arrest, he is required to take protracted psychotherapy and disulfiram. If he fails again, he is put into an insti-

tution for three months. It is reported that the alcoholism rate has fallen in Czechoslovakia.

#### Information and Education

The influence of information and education on motivation in the patient is as yet uncertain and too unreliable for the physician to depend upon. It is only an impression that the education carried on by the National Council on Alcoholism and other antialcoholism agencies has helped, but it has not been determined whether this information and education has produced the results intended. This point has been highlighted by the recent activity with regard to smoking. An appraisal a year after the report of the Surgeon General on the adverse effects of smoking indicated that smoking decreased at first, but later returned to the old levels.<sup>25</sup> It is obvious, therefore, that "scare techniques" or reliance on the individual's doing what is best for him are not adequate methods.

Cigarette advertising has been criticized but no facts have been brought forward to attest the adverse effect of such advertising. In some of our own work on this subject, we found that when drinking, alcoholics responded to the pictures of liquor in liquor advertising, but that dry alcoholics, when asked to describe the advertisements, omitted mention of the prominently displayed liquor.<sup>14</sup> We considered this due to unconscious denial. Denial requires energy to maintain the purposive exclusion of fact, and therefore impoverishes the ego. The maintenance of abstinence by denial is a difficult task, which may help explain the persistent personality problems in abstinent alcoholics and members of Alcoholics Anonymous.

#### Conclusion

An understanding of motivation will enable the physician to comprehend ambivalences in society, in himself and in alcoholics and to reach that state of objectivity which is the most important factor in the treatment of the alcoholic patient.

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# Infectious Hepatitis in California

## A COMMUNITY-WIDE EPIDEMIC

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WILLIAM H. CLARK, M.D., M.P.H., HENRY A. RENTELN, M.D., M.P.H.

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■ *In an epidemic of infectious hepatitis in a rural California community during 1961, 514 cases were reported among 8,166 residents. A sample of the 396 cases reported up to 1 September was studied, and only about a third of these cases could be confirmed in retrospect. A community survey indicated that the attack rate for the first eight and a half months of 1961 was slightly over 3 per cent.*

*Unusual epidemiologic features of what was thought to be a contact epidemic included a summer peak, a preponderance of young and middle-aged adults, a relative sparing of lower socioeconomic groups and mildness of the illness with jaundice appearing in a minority of cases. Secondary cases were rarely observed within the expected 10- to 50-day incubation period.*

INFECTIOUS HEPATITIS reached a record high incidence in the United States in 1961, with over 72,000 cases reported.<sup>11</sup> California, with over 6,000 cases,<sup>2</sup> was one of many states participating in this nationwide increase. In a day of declining morbidity and mortality caused by communicable diseases, viral hepatitis stands out as a mounting problem.

Many outbreaks have been described in the past, including early military epidemics going back as far as the War of 1812 in this country.<sup>1</sup> Recent emphasis has been upon studies in closed or limited populations<sup>8</sup> often having features conducive to the spread of the disease. This paper describes a large epidemic occurring in a community in cen-

tral California in 1961 involving an "open" population, with little control over the many variables which need to be considered in the epidemiology of hepatitis.

### Background

The community involved had a 1960 census population of 5,272, while its entire urban-rural census area contained 8,166 inhabitants. The town is far removed from the major north-south highways. Its economy centers about agriculture. The population is predominantly of Italian and Portuguese extraction, and the standard of living is relatively high. The area has hot, dry summers. The town has a municipal water supply, while the surrounding rural area relies on individual wells. Practicing in the town are five physicians, the only ones within a radius of about 20 miles. Four of the five participated in the reporting of cases.

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Submitted 2 December 1965.



The community had been experiencing an increase in reported hepatitis for some time before this outbreak. On the basis of a statewide attack rate of about 31 reported cases per 100,000 population in 1960,<sup>3</sup> only two or three cases would have been expected, but 22 were reported. This pattern of increased but sporadic cases continued through early 1961. In the spring a further increase was noted, but the incidence decreased again in early June. From late June through early August, over 300 cases were reported, often belatedly as the physicians became more aware of the epidemic. It was at this time that the State Health Department began its investigation.

## Methods

The first phase of the investigation involved the reported cases. Individual morbidity report cards submitted by physicians to the county health department were analyzed for the epidemic period. The patients in all cases reported in 1961 with onset before 1 June were selected for interview, as was a 25 per cent systematic sample of patients with onset after 1 June, reported to the county health department as of 1 September.

Interviews were carried out with the use of a schedule. In addition to family information, there was provision for recording date of onset, symptoms and course of illness, relationship to other cases, recent transfusions or other injections and recent gamma globulin injection. Similar information was gathered for all household members. Laboratory data and results of physical examinations were recorded on the same form after physicians' records had been examined; however, information regarding physical signs was largely lacking.

The second phase of the investigation consisted of a household survey. For practical reasons, only the town proper was surveyed. Since the attack rate based on reported cases was roughly equal in urban and rural sections, this restriction was not felt to be significant. Every 35th household (starting with a random number) was chosen from the city's water meter register, giving 47 index households. At each site, the index household and the two closest neighboring households were to be interviewed.

The purpose of the survey was threefold: (1) to estimate the attack rate in the town; (2) to determine whether the relative paucity of cases in the low socioeconomic area of town might reflect that medical care was unavailable or was not

sought; and (3) to assess the significance of attendance at social events and the frequency of contact with persons who had hepatitis.

A schedule was devised for the survey, on which was recorded for each household member the usual household information, plus note of any recent injection of gamma globulin, all visits to physicians in 1961, all illnesses in 1961, any symptoms compatible with hepatitis, date of onset and course if ill, whether laboratory tests for hepatitis were done, social events attended in 1961, and contacts with persons who had hepatitis. The survey was conducted by two of the authors on 19 and 20 September 1961.

## Diagnostic Criteria

The disease under study appeared to be viral hepatitis on the basis of the characteristic clinical manifestations noted in many cases; however, the majority of the cases were mild. Faced with the problem of uncertainty in diagnosis, the investigators drew up criteria for inclusion as a case, based on the information obtainable in retrospect. The criteria were applied to individuals only after all information had been gathered.

Three diagnostic categories were used:

1. *Supported, or confirmed, clinical cases* were those in which the person had an illness characterized by the presence of at least one of the following major signs, symptoms, or laboratory findings: Jaundice, dark urine, pale stools, tender palpable liver and bile in the urine.

2. *Subclinical infections* were attributed to those persons who had neither signs nor symptoms, but who had bile in the urine.

3. *Unsupported, or unconfirmed, cases* included all those that did not fulfill the criteria of either a confirmed clinical case or a subclinical infection. Because of the strictness of the diagnostic criteria chosen, it is probable that a number of persons who actually had hepatitis were included in this third category.

## Findings

In retrospect, it was possible to reconstruct some of the early stages of the epidemic. On 28 February 1961, a 12-year-old Italian girl arrived at the San Francisco International Airport from her homeland, accompanied by her mother. They proceeded by car to a large ranch eight miles from the town that later was struck by the epidemic. The ranch is the area's largest and is operated by four

families, including that of the girl. Observers attest that the girl was jaundiced when she arrived in the United States; in fact, she had been ill while still in Italy. On 22 March a young woman, a member of one of the families owning the ranch, became ill. Icterus was noted a few days later. In mid-April several additional cases of what now seems to have been hepatitis became evident among these four families.

The young woman, Mrs. X, was put in hospital in one of the clinics in town in late March. In mid-April the wife of one of the physicians who operate this clinic, a close friend of Mrs. X and a frequent visitor to the ranch, had the first symptoms of hepatitis. While Mrs. X was in hospital she had a roommate, a woman from an adjacent county, who also had hepatitis. The feeling existed in the clinic that hepatitis was "not very

contagious," and isolation procedures were not followed closely. In late April, hepatitis began appearing among the clinic personnel. Of about 20 employees, all but two or three had illnesses resembling hepatitis. Gamma globulin was administered to them in late April, but many were already in the prodromal stage of the disease.

Thus on a high "endemic" level of the disease which had prevailed in the community for at least a year, there were superimposed focal outbreaks on a ranch and in one of the town's clinics.

#### Reported Cases

Five hundred fourteen cases with onset in 1961 were reported from the town and its surrounding rural area. The epidemic curve based on these cases is shown in Chart 1. Seventy-two per cent of the 491 patients of known age were at least 20 years old. This preponderance of adults remained constant throughout the epidemic. Females outnumbered males 280 to 234.

Residence could be established as urban or rural in 495 of the 514 cases. There were 325 residents within the city limits and 170 outside. The attack rates for the year (based on the 1960 population since 1961 figures were unavailable) were 6.2 per cent for the urban population and 5.9 per cent for the rural, not counting the 19 with unknown residence. The patients with known street addresses were concentrated almost entirely in the "better" half of the town south and west of the railroad track. The "poor" half of town had a remarkably small number of reported cases.

#### Patients Interviewed

One hundred forty-four patients were interviewed. The group with onset before 1 June was

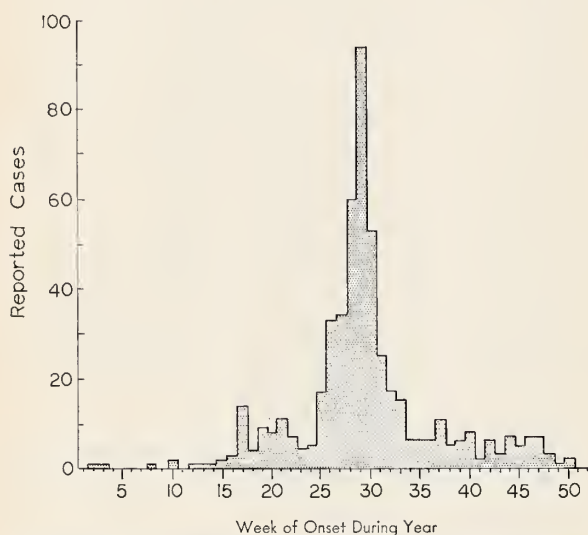


Chart 1.—Reported cases of infectious hepatitis in community and surrounding area by week of onset.

TABLE 1.—Comparison of Interviewed and Reported Cases by Sex, Age, and Urban-Rural Residence

	Cases Interviewed Onset Before June		Cases Interviewed Onset After June 1 (25 Per Cent Sample)		All Reported Cases June 1-Sept. 1		All Reported Cases—1961	
	Number	Per Cent	Number	Per Cent	Number	Per Cent*	Number	Per Cent*
Sex—								
Male .....	28	47	36	43	174	48	234	46
Female .....	32	53	48	57	188	52	280	54
Age—								
Under 20.....	15	25	19	23	104	30	139	28
20 & Over.....	45	75	65	77	243	70	352	72
Unknown .....	0	0	0	0	15	....	23	....
Residence—								
Urban .....	35	59	60	71	245	68	325	66
Rural .....	25	41	24	29	113	32	170	34
Unknown .....	0	0	0	0	4	....	19	....

\*Cases in "Unknown" category excluded from the calculation of per cent.



seen essentially *in toto* (60 cases out of 61). From the larger group of patients with onset after 1 June, 84 of the 25 per cent sample of 85 were interviewed. Table 1 shows the distribution of the interviewed patients and the reported cases by sex, age, and urban-rural residence. None of the differences between the sample and the entire late group approached statistical significance.

#### Confirmed Cases

The diagnostic criteria outlined previously were applied to interviewed patients. Calculations made on the basis of 396 cases represented ( $60 + [84 \times 4] = 396$ ) revealed that 37 per cent of the reported cases could be confirmed, 11 per cent could be classified as subclinical infections, and 52 per cent rejected as unsupported. Seventy-three per cent of the early (before 1 June) cases were confirmed, however, compared with 30 per cent of the later ones. Much of the difference in confirmability between early and late cases is accounted for by contrasts in the reporting methods used by the several physicians. One particular physician's share of reported cases increased as time passed, and the relative non-confirmability of diagnosis among the cases he reported tended to lower the overall confirmability percentage.

Chart 2 presents the epidemic curve based on confirmed cases only. The abrupt truncation is an artefact caused by sampling only those cases reported before September 1. Since the curve based on reported cases shows a decline after this time, it may be assumed that a curve based on "confirmed" cases would have shown a similar decline, had the study been done at a later date.

Twenty-three (52 per cent) of the patients in the early confirmed cases and 12 (48 per cent) in the late confirmed cases were jaundiced. Taking into account the effect of partial sampling of the late cases, the overall rate of jaundice was calculated to be 49 per cent. Table 2 presents the symptoms reported in the confirmed cases.

#### Other Information Obtained from Case Interviews

Although households having two or more cases among their members were frequently encountered, calculation of secondary attack rates was not possible because cases associated with a household were usually either co-primary (*i.e.*, onset less than 10 days apart) or several months apart.

Gamma globulin was given to an estimated 40 to 45 per cent of household contacts of reported

TABLE 2.—Symptoms in Confirmed Cases

Symptom	Icteric Cases		Anicteric Cases	
	Number	Per Cent	Number	Per Cent
Anorexia .....	26	74.3	22	64.7
Nausea .....	22	62.8	22	64.7
Abdominal pain .....	22	62.8	23	67.6
Fever .....	22	62.8	17	50.0
Dark urine .....	21	60.0	23	67.6
Vomiting .....	14	40.0	9	23.5
Sore throat .....	9	25.7	8	20.6
Pale stools .....	3	8.6	2	5.9
Total .....	35	100.0	34	100.0

cases during the epidemic. Seventy-nine per cent of 184 contacts of reported cases before June were given such protection compared with 35 per cent of 191 household contacts of reported cases with later onset—persons who represent a much larger group.

#### Community Survey and Attack Rates in Various Community Groups

One hundred forty-one households were chosen for inclusion in the survey, of which 128 (91 per cent) were actually included. The 128 households contained 441 persons, 8 per cent of the town's population at the time of the study. Thirty-one (7 per cent) of these persons had been reported as having hepatitis. This figure is in close agreement with the urban attack rate of 6.2 per cent based on all reported cases. These 31 persons were evaluated on the same basis as the patients chosen for interview in the earlier study, insofar as information was available from the patient. (Ten of the 31 in fact had been included in the earlier interviews.) Laboratory data were generally not available for individuals seen in the community survey, nor were physical findings.

Eleven of the 31 reported cases encountered in the survey were considered to be confirmed on the basis of the somewhat restrictive criteria utilized; in addition, three cases were found which had not been reported but which satisfied the diagnostic criteria. This represents an attack rate of slightly

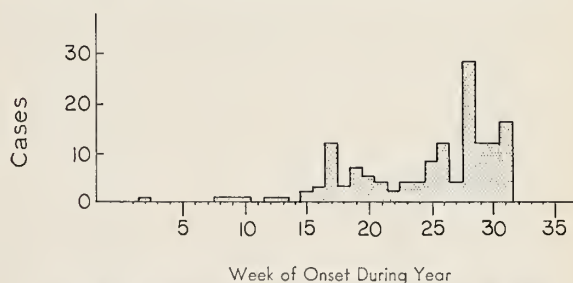


Chart 2.—Confirmed clinical cases by week of onset.

TABLE 3.—*Attack Rate Among Survey Population by Economic Rank*

	Economic Rank				Total
	1	2	3	4	
Number of Households .....	28	52	29	19	128
Percentage of Households .....	22	41	23	15	.....
Households with Cases .....	4	6	0	0	10
ATTACK RATE (HOUSEHOLD) .....	14.3%	14.6%	0.0%	0.0%	7.8%
Number of Individuals .....	110	168	102	61	441
Percentage of Individuals .....	25	38	23	14	.....
Number of Cases .....	5	9	0	0	14
ATTACK RATE (INDIVIDUAL).....	4.5%	5.4%	0.0%	0.0%	3.2%

over 3 per cent for the first eight and a half months of 1961.

#### Economic Rank

Each household in the survey was assigned a rank, from a high of one to a low of four, to approximate its economic condition. This rank was based on the appearance of the structure and the neighborhood, and in borderline cases a rank was agreed upon by both interviewers. Cognizance is taken of the limitations of this method. Table 3 shows that 63 per cent of the households in the sample were assigned to ranks one and two, reflecting the high standard of living in the town. Cases included in Table 3 are all those considered confirmed by the investigators, whether reported or not. No cases were found among persons in the two lowest economic groups. The probability that this would occur by chance alone is less than .005.

Since two of the five diagnostic criteria (tender palpable liver and bile in the urine) require a visit to a physician for their detection, it might be thought that the absence of cases in Groups 3 and 4 reflects that persons in the low economic groups did not seek medical attention, rather than any real difference in disease incidence. Examination of the 14 confirmed cases in Groups 1 and 2 shows that dark urine, white stools, and/or jaundice (criteria not requiring medical attention for their detection) were present in 12 of the 14. When the

analysis is restricted to these 12 cases, the difference between the upper and lower groups is statistically significant ( $p < .01$ ).

#### Household Size

Attack rates were calculated for households of various sizes. Over 78 per cent of the cases occurred in households of three or four persons, although only 45 per cent of the persons surveyed lived in households of those sizes. Households of smallest and largest sizes, which were generally ranked low economically, had low attack rates.

#### Sex and Age

The composition of the survey population is shown in Table 4 and is compared with 1960 census figures. Age composition of the four economic ranks varied considerably. Although females outnumbered males slightly among reported cases throughout the epidemic, the community survey revealed similar attack rates for the sexes.

Attack rates by 15-year age groups are presented in Chart 3. A similar curve based on confirmed reported urban cases is also given in the chart. It is evident in both instances that the 0-14 age group had a relatively low attack rate, while the highest attack rate was in the 30-44 age group.

#### Attendance at Social Gatherings

The attack rates among the 100 persons in the survey who attended large social gatherings was

TABLE 4.—*Composition of Survey Population by Age and Sex*

	Percentage of Group Which Was:						
	Male	Female	0-14	15-29	30-44	45-59	60+
1960 Census							
(Entire Community) .....	49.8	50.2	33.9	16.4	21.9	15.6	12.2
Survey Population .....	53.7	46.3	33.3	19.5	20.4	15.0	11.8
Economic Rank 1 .....	53.6	46.4	40.9	10.0	34.5	12.7	1.8
Economic Rank 2 .....	51.2	48.8	27.4	25.6	17.3	18.5	11.3
Economic Rank 3 .....	57.8	42.2	32.4	20.6	17.6	12.7	16.7
Economic Rank 4 .....	54.1	45.9	37.7	18.0	8.2	13.1	23.0



6 per cent, compared with a rate of 2.3 per cent among those not reporting attendance at such events. The difference is not statistically significant.

#### Contact with Persons Who Had Hepatitis

Eleven of the 152 persons in the survey who recalled contact with a person having hepatitis had themselves had the disease—a 7.2 per cent attack rate. Among those without a history of such contact, the attack rate was only 1.0 per cent. The difference is highly significant statistically ( $P < .005$ ). Part of this difference in attack rates may be explained on the grounds that persons with hepatitis presumably would recall their contacts more accurately than those who were not ill.

#### Description of Cases

Of the 14 persons with confirmed cases in the survey population, four, or 29 per cent, were jaundiced. The most common symptoms were anorexia, nausea, and dark urine (85 per cent) and abdominal pain (78 per cent). The mean duration of illness was 4.3 weeks.

#### Discussion

Despite the large number of descriptions of outbreaks of infectious hepatitis already in the literature, this community-wide epidemic is thought to be worth reporting because of the unusual epidemiologic features.

Initially the possibility of a common-source epidemic was raised because of the large number of reported cases occurring within a relatively short time. Evidence for a common source of exposure was looked for but not found. County health department sanitarians had monitored the municipal water supply closely throughout the year and

found it to be bacteriologically satisfactory. Furthermore, the urban and rural areas, which had had similar attack rates, did not receive their water from the same source. Four creameries operating in the town were investigated. Some breaches in good sanitary technique were found to have occurred, and two creamery employees were known to have been ill. The role, if any, of these two persons in the transmission of infection remains undetermined, but there was no evidence that they contributed to the spread of the epidemic. A third possibility, that of spread by a food handler at one or more of the large parties, seems untenable as an explanation of a prolonged epidemic involving numerous persons not attending such gatherings.

The question of person-to-person spread was then considered. The failure to find more than an occasional secondary case occurring in household contacts tends to argue against this mode of spread. The findings of the community survey, on the other hand, lend support to it, since the attack rate experienced by persons recalling contact with someone with hepatitis was seven times that experienced by persons without a history of such contact. Admittedly the situation is somewhat unsatisfactory; nevertheless, it was concluded on the basis of the available evidence that the epidemic was spread by person-to-person contact. The epidemic curve shown in Chart 2 is entirely compatible with such a mode of transmission.

Although epidemiologically infectious hepatitis is not completely understood, it is evident that the present epidemic differs in several important respects from the usual contact epidemic of hepatitis.<sup>10</sup> Comparable outbreaks<sup>5-7,9</sup> have generally conformed to the classical pattern, with most of the cases occurring in the cooler months among school-age children. The clinical spectrum in these epidemics has included mild to severe, occasionally fatal, cases, but icterus has been noted in most cases. The incubation period has usually been about four or five weeks, as calculated by secondary attack rates. A relatively low economic status, with less than ideal water and sewage systems, has often been associated with hepatitis epidemics.

In contrast, the epidemic described here was essentially a spring-summer event which affected far more young and middle-aged adults than children, mainly in the areas of high living standard.

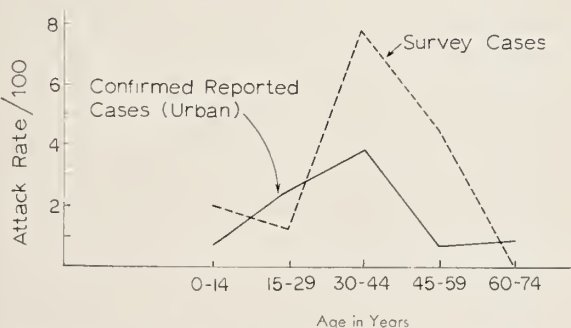


Chart 3.—Age-specific attack rates, confirmed reported urban cases and survey cases.

Most of the illnesses were comparatively mild, with jaundice in a minority of cases. Household secondary attack rates and average incubation period could not be calculated because virtually no secondary cases occurred in households within the expected 10- to 50-day interval.

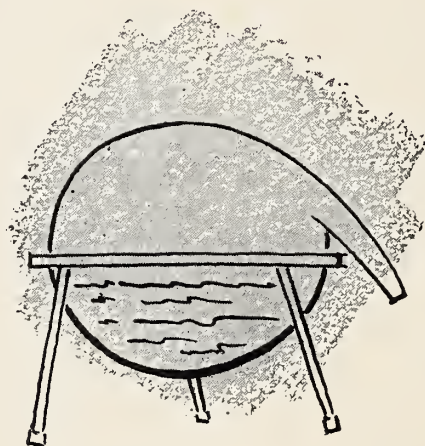
Until such time as specific diagnostic procedures (virus isolation and serologic techniques) are developed for infectious hepatitis, one can merely speculate regarding the reasons for such pronounced epidemiologic differences. It is perhaps not unreasonable to postulate that an immunologically distinct strain of hepatitis virus A,<sup>4</sup> which is relatively avirulent, was involved in this outbreak, resulting in numerous subclinical infections which served to perpetuate the epidemic over a period of months and permitted the majority of infections in young children to go undetected.

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# Growth Hormone Studies In Growth Retardation

## *Therapeutic Response to Administration of Androgen*

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■ *Growth hormone assays were performed before and after androgen administration in a 12-year-old boy with unexplained growth retardation. A subnormal growth hormone secretion in response to a standard hypoglycemic stimulus was demonstrated, and it was corrected by androgen pretreatment. After that, a normal serum growth hormone level and a temporary growth spurt were demonstrated.*

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GROWTH RETARDATION is a feature common to several abnormal conditions in children. It is usually secondary to undernutrition or a chronic non-endocrine disorder, but there remains a significant number of children whose small size cannot be ascribed to such causes. The differential diagnosis of this group is usually between pituitary and "constitutional" dwarfism.<sup>4</sup> The diagnosis of pan-hypopituitarism can generally be made after appropriate studies and a period of observation. However, the role of a unihormonal deficiency of somatotropin in growth failure has not been clearly delineated. Brasel and coworkers<sup>3</sup> called attention to the fact that deficiencies of tropic hormones may occur in any combination and that isolated deficiencies of somatotropin may well occur. The diagnosis of constitutional or genetic dwarfism has no precise boundaries. This clinical entity frequently is indistinguishable from hypopituitarism on the one hand, and blends into the spectrum of uncom-

plicated delayed adolescence on the other. It seems reasonable to hypothesize that many children who have been classified as constitutional dwarfs or "late developers" usually may have a defect in the production or the release of growth hormone.

Stormont and coworkers<sup>12</sup> demonstrated that children clinically classified in these categories of growth retardation can be stimulated to an increased growth potential by the administration of a variety of hormonal agents. This suggests that if a defect in the growth hormone mechanism exists in such cases, it must be a partial one and capable of responding to other endocrine influences.

The advent of a sensitive radioimmunoassay for growth hormone<sup>7</sup> and the demonstration that induced hypoglycemia serves as a potent stimulus to secretion of growth hormone<sup>9</sup> now permit a more exact approach to these problems. This report describes the study of somatotropin secretion in response to a standard hypoglycemic stimulus before and after androgen pretreatment in a child with unexplained growth retardation.

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Submitted 27 December 1965.

## Report of a Case

A boy 11 years and 10 months of age was seen because of short stature (Figure 1), which had concerned the parents for many years. The mother had been advised by numerous physicians either that her son eventually would grow "normally" or that his growth was within normal limits. The family's inability to accept these statements led to the patient's referral to the Pediatric Endocrinology Clinic at Letterman General Hospital.

In early infancy, the patient had had frequent respiratory distress and vomiting. These symptoms together with infantile eczema were thought to be of allergic origin. Throughout the first two years of life he received a strict hypoallergenic diet with vitamin and iron supplements. Thereafter, the diet was less restricted and, after age four, he resumed a normal diet. The only allergic manifestation after that was an indolent atopic dermatitis that was controlled with local medications. He has had no unusual or frequent illnesses.

He was considered the product of a normal 39-week pregnancy, having a birth weight of 7 lb 5 oz.

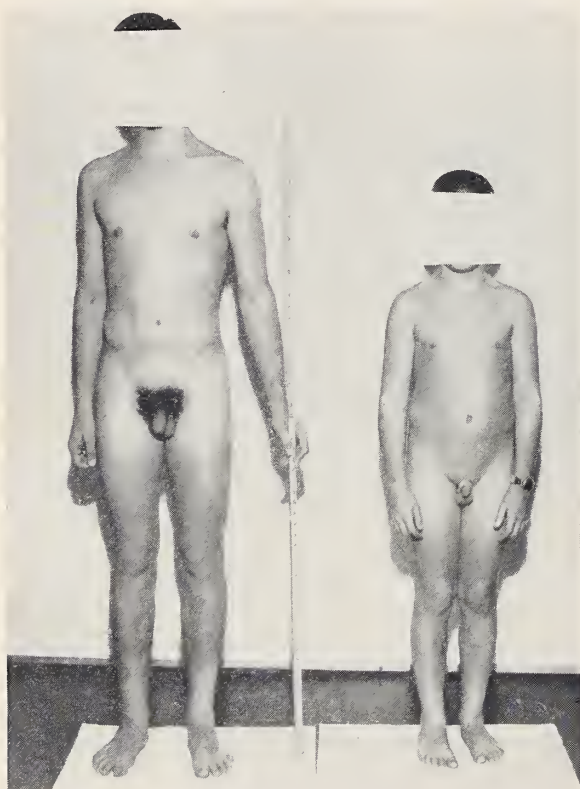


Figure 1.—Patient with retarded growth (right), age 11 years 10 months, and his normally developed brother, age 13 years 1 month.

At age one he weighed 22 lb (50th percentile on the Stuart Anthropometric Chart) and his length was 30.3 inches (50-75th percentiles). At one and a half years weight was 24 lb (25-50th percentiles) and length 33 inches (50-75th percentiles). Measurements taken between ages two and six are not available. Height measurements for subsequent years were regularly between the third and tenth percentiles and weight measurements were between the 50th and 75th percentiles. Skeletal ages, estimated from wrist roentgenograms, at one and a half, three and six and a half years were considered retarded. Thyroglobulin (Proloid®) was administered orally for several months in the second year of life without laboratory confirmation of hypothyroidism. No growth spurt occurred. With this exception, no therapy for short stature was given before the patient was referred to our clinic.

The patient's mother, father and maternal grandfather are in the 50th percentile for height. A brother, 15 months older, was pubescent and at the 97th percentile for height and weight. He, too, had had eczema. There was no family history of unusual body size, endocrine dysfunction or other diseases that might affect growth.

The patient was alert, cooperative and of normal proportions, but appearing younger than his stated age. His weight was 82 lb (50th percentile) and height 54.8 inches (third to tenth percentiles). There were no signs of pubescence and, other than short stature, no significant abnormal physical findings.

Hematocrit, total leukocyte count and cell differential, sedimentation rate and routine urinalysis were within normal limits. The fasting blood glucose was 87 mg per 100 ml. Serum protein-bound iodine was 7.7  $\mu$ g per 100 ml. Results of 24-hour urinary hormone excretion studies were: 17-ketosteroids, 5.3 mg; 17-hydroxycorticosteroids, 2.8 mg; testosterone, less than 5  $\mu$ g; follicle stimulating hormone activity, positive at 50 but negative at 80 mouse units. Skull roentgenograms were considered normal. Wrist roentgenograms taken to estimate skeletal age were interpreted as retarded, consistent with age 10 at actual age 11 years, 10 months.

*Special Studies.* The patient was in hospital three days for initial studies. He was given a regular diet and permitted ward activity except during two consecutive insulin tolerance tests. A general endocrine survey and growth and development



profile were obtained during the first hospital day. The results of these studies are recorded above. As a standard stimulus for growth hormone secretion, 0.1 unit of regular insulin per kilogram of body weight was administered after an overnight fast for each of the growth hormone studies.

A control test was performed without previous medication. Blood was obtained for glucose and growth hormone analysis at 15- to 30-minute intervals for two hours after insulin administration. The test was repeated the next day, after administration of 400 mg testosterone propionate intramuscularly 20 hours before, and giving 10 mg methyltestosterone sublingually 20 minutes before and again immediately preceding the insulin infusion. Blood samples were obtained as above.

True blood glucose was determined by a glucose oxidase method<sup>10</sup> and growth hormone was measured by the radioimmunoassay of Hunter and Greenwood<sup>7</sup> as modified by Grodsky to employ growth hormone-I<sup>125</sup>, separating bound and free hormone by preferential precipitation with Na<sub>2</sub>SO<sub>4</sub>.<sup>6</sup>

A growth chart was kept from the initial study to the time of this report. It encompassed five months of observation: the immediate two-month postandrogen test period, a subsequent one-month period of treatment with oral fluoxymesterone (Halotestin®) and another two-month span without any therapy. Five months after the initial test series, the insulin tolerance test was repeated.

Results

The initial growth hormone response pattern is shown in Table 1. A brisk hypoglycemic response was found at 30 minutes, demonstrating normal insulin sensitivity. The growth hormone response was negligible when compared with values for normal postpubescent subjects<sup>6</sup> and for normal prepubescent individuals.<sup>8</sup>

The "testosterone-primed" growth hormone response is shown in Table 2. Again a brisk hypo-

TABLE 2.—Growth Hormone Response to Standard Insulin Tolerance Test (0.1 units per kilogram) with Testosterone Pretreatment

Time (minutes)	Glucose (mg/100 ml plasma)	Growth Hormone (mµg/ml serum)
0 .....	95	2.7
30 .....	43	22.5
45 .....	97	23.5
60 .....	80	17.5
90 .....	111	26.5
120 .....	136	4.8

glycemic response occurred within 30 minutes. The growth hormone levels rose sharply to peak values 10 times greater than the fasting level. This response was maintained for 90 minutes. Seventy days after administration of the testosterone propionate, the patient's height had increased from 54.8 inches to 56.5 inches (25th percentile) and weight from 82 lb to 87.5 lb (50th percentile). Slight growth of pubic hair was evident.

The patient was then given fluoxymesterone orally, 2.0 mg per day for 30 days. This treatment was followed by 50 days without therapy. During this 80-day period his height remained the same and he gained 3 lb. There was no further change in secondary sex characteristics.

Insulin tolerance testing at this juncture resulted in a normal growth hormone response to hypoglycemia (Table 3). Urinary steroid determinations were unchanged from previous values.

Discussion

The role of the somatotrophic hormone in patients with growth delay is undefined. Reports have appeared attesting growth stimulation in such children with androgenic hormones, but the exact mechanism for this observed phenomenon is unknown.<sup>11,12</sup>

The results of the initial insulin tolerance test in the present case show clearly that the patient had a subnormal level of growth hormone which did not respond normally to the hypoglycemic

TABLE 1.—Growth Hormone Response to Standard Insulin Tolerance Test (0.1 units per kilogram)

Time (minutes)	Glucose (mg/100 ml plasma)	Growth Hormone (mµg/ml serum)
0 .....	125	0.5
30 .....	34	2.2
45 .....	85	0.5
60 .....	106	0.5
90 .....	108	0.5
120 .....	115	1.9

TABLE 3.—Growth Hormone Response to Standard Insulin Tolerance Test (0.1 units per kilogram) Five Months after Initial Study

Time (minutes)	Glucose (mg/100 ml plasma)	Growth Hormone (mµg/ml serum)
0 .....	95	5.8
30 .....	39	9.0
45 .....	75	19.5
60 .....	92	16.5
90 .....	101	12.5
120 .....	113	6.3

stimulus, although he did have assayable growth hormone. The administration of testosterone appeared to be a potent stimulus to the somatotrophic center and prompted a brisk response in serum growth hormone, reflected both in the basal value and in augmented secretion after the hypoglycemic stimulus. This augmentation was subsequently demonstrated upon testing after two months without any therapy.

The growth hormone response to testosterone administration suggests that there is a direct interplay between this gonadal hormone and the pituitary growth hormone releasing system. This effect may be mediated through a hypothalamic mechanism, as was recently proposed by Abrams and coworkers.<sup>1</sup>

This information does not settle the question of the therapeutic usefulness of these hormones in problems of growth retardation. Although there appears to be an augmented growth hormone response after androgen administration, as demonstrated by this study, this is not the only effect of such therapy. Bayley and coworkers<sup>2</sup> and Goldzieher<sup>5</sup> called attention to the greater increase in skeletal maturation than height age in prepubertal children who were given testosterone. Early epiphyseal closure is a definite risk in androgen therapy.

Standard test procedures for growth hormone stimulation coupled with pretreatment schemes with various sex hormones in a number of patients with problems of growth delay are now in progress.

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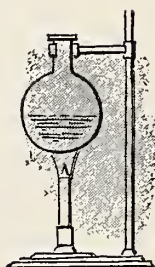
Generic and Trade Names of Drugs.

Thyroglobulin—*Proloid*.

Fluoxymesterone—*Halotestin*.

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# Therapeutic Utilization of the Diurnal Variation in Pituitary-Adrenocortical Activity

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■ *The degree of pituitary-adrenocortical suppression resulting from exogenous corticosteroid is related to the time of day the steroid is administered. Morning administration has less effect and evening administration a greater effect than do divided doses given over the course of the day.*

*Clinical studies have shown that in the great majority of patients with corticosteroid responsive diseases, an intermittent dosage schedule is at least as effective as is administration of an equal dose in a three or four times a day regimen. Other undesirable side effects of corticosteroid therapy may also be decreased by an intermittent schedule. It is suggested that the customary divided dosage schedule for corticosteroid administration be replaced with an intermittent regimen, the medication being given in the morning. This may be once a day, or, if therapeutic results are satisfactory, once every other day.*

RECENT REPORTS have indicated that intermittent therapy with corticosteroids has less suppressive effect on the pituitary-adrenocortical axis than does the administration of the same amount of steroid in divided doses over the day. As part of our investigation of different regimens of corticosteroid administration, we have studied the dynamics of this pituitary sparing.

## Material and Methods

Flumethasone,\* a newly developed glucocorticoid of high potency, was administered to three normal male volunteers as a single daily dose of 0.75 mg. This dose was selected because previous experiments had shown that 0.75 mg, given in divided doses over the 24-hour period, would re-

sult in a mean 50 per cent suppression in urinary 17-hydroxycorticosteroid (17-OHCS) excretion.

In each therapy period flumethasone was administered orally for four days at one of three times: 8 a.m., 4 p.m. or midnight. Courses of therapy were random; they were separated by at least one week without treatment. During each therapy cycle, 24-hour urine collections were made on the two days preceding flumethasone administration and on the last two days of therapy.

Urinary 17-OHCS excretion was determined by the method of Silber and Porter.<sup>11</sup> Creatinine determinations were concurrently performed to assure completeness of the collections.

## Results

The results are presented in Table 1. The mean excretion of 17-OHCS on the two days immediately preceding treatment is compared with the mean excretion on the last two of the four days of flu-

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\*Flumethasone (6 $\alpha$ ,9 $\alpha$ -difluoro-16 $\alpha$ -methyl-11 $\beta$ ,17 $\alpha$ ,21-trihydroxy- $\Delta^1,4$ -pregnadiene-3,20-dione).

methasone administration. The results are expressed as per cent suppression. A trend is apparent. Administration of flumethasone at 8 a.m. resulted in a 40 per cent decrease in 17-OHCS excretion over the ensuing 24 hours, administration at 4 p.m. in a 61 per cent decrease, and administration at midnight in an 83 per cent decrease. The difference between the suppression resulting from a single dose at 8 a.m. and at midnight is significant at  $P < .01$  level of confidence as determined by Student's *t* test. These observations may also be compared to the mean 50 per cent suppression when the same dose of flumethasone was administered in divided doses to another group of normal subjects.

## Discussion

DiRaimondo and Forsham<sup>2</sup> suggested some years ago that 10 mg of prednisone administered at 8 a.m. caused less suppression of adrenocortical activity than did 2.5 mg administered every six hours around the clock. While this manuscript was in preparation Nichols and coworkers<sup>7</sup> reported that 0.5 mg of dexamethasone caused only partial suppression of cortisol secretion when administered at 8 a.m. or 4 p.m., but virtually complete suppression for a full 24-hour period when administered at midnight. Martin and Hellman<sup>6</sup> reported that the response to methopyrapone is also greatest in the hours immediately after midnight. Methopyrapone response is dependent on the sensitivity of the hypothalamus to decreased concentrations of circulating corticosteroid. It would appear that the response to feedback stimuli is temporally concentrated in the early morning hours when the diurnal burst of adrenocorticotropin (ACTH) secretion normally occurs. Neither an increase nor a decrease in circulating corticoid concentration at other times of the day has much effect.

The therapeutic implications with regard to maintenance of normal reactivity of the hypothalamic-pituitary-adrenal axis are obvious. Administration of glucocorticoids in the treatment of corticosteroid responsive conditions should be early in the morning, so that when the pituitary is ready for its next diurnal surge of ACTH secretion the administered corticosteroid will no longer be circulating in concentrations high enough to block it. The actual concentration still circulating at any time after administration will depend on several factors, including the biological half-life of the steroid and the size of the dose administered. Any investigation of the pituitary suppression resulting from different corticosteroid regimens must take these variables into consideration. If very large doses are therapeutically required, or if the duration of action of the steroid is especially prolonged, as appears to be true of some of the synthetic fluorinated corticosteroids, the pituitary suppressing activity of the exogenous corticoid may persist for 24 hours or longer. An every-other-day regimen of administration as suggested by Harter and coworkers,<sup>5</sup> or another intermittent schedule such as three to five successive days of each week may be required to permit pituitary escape. Morning administration would be less suppressive with these dosage regimens as well.

The application of these concepts to prevention of other undesirable side effects is less clear-cut. In the case of pituitary suppression, we are dealing with a peculiar diurnal variation in its sensitivity to feedback influences. If the same amount of exogenous glucocorticoid is needed to gain a given therapeutic goal with either once a day or divided dosage schedules, we are probably getting a net excess of administered corticoid in the once-a-day regimen, since in this situation the endogenous secretion will supplement the exogenous administration. The great variation in incidence of any

TABLE 1.—Urinary 17-OHCS† (in mg per 24 hours) in Three Subjects Receiving the Same Dose of Flumethasone at Different Times of the Day

Flumethasone 0.75 mg by mouth at	Urinary Excretion of 17-OHCS in 24 Hours								
	8 a.m.			4 p.m.			Midnight		
	Control	Rx	Per Cent Decrease	Control	Rx	Per Cent Decrease	Control	Rx	Per Cent Decrease
Subject A .....	9.7	4.5	46	12.5	2.9	77	9.4	2.2	77
Subject B .....	7.8	5.0	36	11.2	2.7	76	6.9	0*	100
Subject C .....	4.6	2.8	39	6.4	4.4	31	7.2	2.1	71
Mean ± SD .....	....	....	40 ± 5	....	....	61 ± 26	....	....	83 ± 15

\*No Porter-Silber chromogen detectable.

†17-hydroxycorticosteroid.

Each control value represents the mean of determinations carried out on the two days immediately preceding treatment. Each Rx value represents the mean of determinations carried out on the third and fourth days of flumethasone administration.



particular corticosteroid side effect makes it difficult to establish whether intermittent therapy or the classical procedure of giving medication in divided doses three to four times daily results in fewer undesirable reactions. The available reports suggest that side effects such as peptic ulceration are less frequent if steroid treatment is given once daily or at less frequent intervals.<sup>1,4,5,9,12</sup> Prospective control studies in large populations are needed to establish this observation on a firm statistical basis.

Dougherty and coworkers<sup>3</sup> demonstrated that inflamed connective tissue concentrates administered cortisol with respect to blood and that the anti-inflammatory activity of cortisol continues to be exerted for a prolonged period after it has disappeared from the tissue. Persistence of the anti-inflammatory effect beyond the time when the anti-inflammatory agent can be measured in the inflamed tissue is not surprising. Many of the metabolic effects of the steroid hormones appear to represent the end result of a long chain of reactions triggered by an effect of steroid on nucleic acid synthesis.<sup>10</sup> The hormone has usually disappeared from the target tissues before changes in enzyme activities can be demonstrated. There is little reason to suspect that constant blood levels of corticosteroid are necessary for this triggering action.

An analysis of the therapeutic effectiveness of intermittent corticosteroid administration must consider the doses used and the duration of action of the individual corticosteroid employed. In general, the effectiveness of once a day therapy appears comparable to the conventional divided-dose regimens in the great majority of patients.<sup>1,4,8</sup> Indeed the same therapeutic end point may be reached with slightly smaller total doses.<sup>4</sup> Alter-

nate day therapy has been effective in the treatment of asthma,<sup>5</sup> dermatologic disorders<sup>9</sup> and nephrosis,<sup>12</sup> but perhaps is not as effective in the treatment of adult rheumatoid arthritis.<sup>8</sup> This may be due to differences in dosage or in the steroids employed in the particular studies, or it may reflect a true difference in the response of the disease to corticosteroids.

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# Cervico-Vaginal Smears

## Cytologic Examination

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■ *Discrepancies among classification systems of Papanicolaou smears and lack of communication between cytologist and clinician are not uncommon. An attempt should be made by the cytologist to estimate, on a percentage scale, the likelihood of any given smear indicating carcinoma. This enables a more realistic and systematic management of a patient whose smear is other than negative.*

*Proper technique in obtaining the smear is essential to proper interpretation, and it must be stressed that a negative smear in a patient with a cervical lesion does not rule out carcinoma. Likewise, a negative smear cannot rule out carcinoma higher in the generative tract.*

SINCE 1928, when Papanicolaou first presented his work on the cytologic diagnosis of cancer, cytologists have sifted through a multitude of potential refinements, always with these goals: better ways to obtain material, better ways to stain the cells and, very important, more accurate ways of classifying the resulting interpretation.

Clinicians have coped with a different problem. Discrepancies among classification systems and differences of opinion in what is the correct interpretation, and what is the proper management of a patient with an abnormal smear have perplexed them. This problem will remain until a thorough understanding between clinician and cytologist has come about.

To treat a patient intelligently, a clinician must be armed with concrete information. He must know, for any given classification, for any one specific smear, what is the calculated percentage of accuracy. How often will a Class III smear have correctly predicted carcinoma? Then, assured by this firmer footing, the next step follows logically, and he can proceed with confidence. Classifications, therefore, are of value in direct proportion to one factor: How well is the cytologist communicating with the clinician?

Vaginal smears are commonly classified by numbers, I through V, with I and II meaning no evidence of malignant cells; V, almost certain malignant change; III and IV, suspicious, and highly suspicious, respectively. A simpler classification—negative, suspicious and positive—estimates the chances in a given case of the patient's having a malignant lesion; and, unlike the number system, it does not hint at unrealistic accuracy. Therefore, at least 10 per cent of "suspicious" reports will be found to have accurately forecasted malignant cervical changes; "positive" must be taken to mean "100 per cent probability" of malignant change. With this information, the clinician must proceed to prove or disprove malignant disease.

In the "suspicious" group—patients with at least a 10 per cent likelihood of having carcinoma—the patient should be reexamined and a repeat smear taken. If the cervix appears normal and the remainder of the pelvic examination discloses nothing more, and the repeat smear is negative, a third smear should be done in three to six months. But if the second smear is again suspicious, a cone biopsy is indicated. There are several circumstances that would require more individualized consideration as to when and if a conization should

Submitted 6 January 1966.



be done. The patient might be (1) pregnant; (2) young and nulliparous; (3) a poor anesthetic risk; (4) very old; (5) have disease other than gynecologic that carries a poor prognosis.

### Technique for Obtaining Smear

The several techniques now used uniformly for obtaining a smear of secretion for examination produce accurate results, but an individual cytologist may have a preference and may feel that one way gives him greater competence in his interpretation. One smear is usually sufficient whether obtained by cervical scraping or sampling the exfoliated cells in the vaginal pool. The vaginal pool method gives a higher proportion of "positives" for endometrial, tubal and ovarian carcinomas.

The technique of preparing the smear is as important as the technique for obtaining it. The material should be spread rapidly—one or two quick strokes—and the slide then should be put *immediately* into a fixative solution. In smears that become dry before being fixed, cells have pale, swollen nuclei, making accurate interpretation more difficult.

### When to Take the Smear

Usually the smear material can be taken at any time, although there are some conditions to be avoided or taken into account.

A smear should not be taken during active bleeding (more than usual menstrual flow). In cases of severe vaginitis, profuse leukorrhea may

so dilute a specimen containing malignant cells that a false negative interpretation could occur.

In the post partum period before menses have been reestablished, ovarian function is deficient and parabasal cells predominate in the smear. Differentiating the parabasal from the malignant cell is no problem, but a smear containing cells all of which have large nuclei, all with a reduced nuclear cytoplasmic ratio could camouflage a cluster of malignant cells.

### Age at Which Smears Should Be Obtained

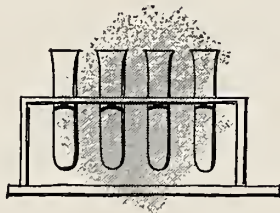
Married women should have smears at any age, and also girls in their late teens, especially if they have gynecologic complaints or a family history of cancer. Teenage patients, too, have carcinoma of the cervix; the younger the age at which periodic cytologic examination is begun, the more often will early cervical malignant disease be diagnosed. Ideally, smears should be taken annually. This is especially important for the woman who has reached her late twenties.

### Warning

Never can a "negative" smear be assumed to rule out carcinoma. Biopsy of any abnormality of the cervix is mandatory, regardless of the cytologic interpretation of a smear of exudate.

In older patients, abnormal bleeding often indicates carcinoma in the generative tract above the cervix. Since a negative smear does not rule out endometrial carcinoma, other diagnostic procedures should be done.

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# Autopsy in California

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■ *From information compiled from death certificates registered in 1952 and 1962 an examination was made of California's autopsy performance and the characteristics of deaths in which autopsy was done. The data indicated that California had an overall autopsy rate of 37 per cent of total deaths in 1962, probably higher than any other state. In the decade reviewed, there was a 62 per cent absolute increase in autopsies and a 7 per cent increase relative to total deaths.*

*Substantial increases in the proportion of deaths in which autopsy was done were found for physician-certified deaths in both metropolitan and nonmetropolitan counties and for coroner-certified deaths in nonmetropolitan counties. For all but two of forty-five selected natural causes of death there were increases in the proportion of deaths in which autopsy was done.*

*Seventy per cent of deaths occurred in some type of facility. About one-half of all deaths occurred in general hospitals, and autopsy was done in 42 per cent of such cases.*

*The dual factors of a high autopsy rate and overrepresentation of deaths brought to autopsy in white males, ages 35-64, support the validity of a reported decline in California's death rate for arteriosclerotic heart disease.*

THE RELIABILITY of California's mortality statistics may be better understood by study of autopsies. If a postmortem examination is made and the results considered by the medical certifier, usually a more accurate and complete statement of conditions leading to death is made on the death certificate. This report presents some detailed information describing the performance of autopsy in California and a demographic analysis of deaths in which autopsy was done. The use of autopsy findings in certifying causes of death on original death certificates and by amendment procedure is also described. The discussion focuses on how the statewide autopsy pattern may effect trends and

differentials in mortality rates for arteriosclerotic heart disease.

## Source and Accuracy of Data

The data on autopsies presented here are compiled from death certificates registered in California for the years 1952 and 1962. Immediately the validity of the source is open to question: How accurately does the death certificate record whether or not an autopsy was performed? McMahan reported that for the United States in 1955 an average of one-sixth of death certificates did not state whether or not an autopsy had been performed.<sup>5</sup> However, California then ranked low in this omission, with only 3 per cent of its death certificates failing to record autopsy status. In 1962, less than 2 per cent of the state's death certificates made that omission.

From the Bureau of Vital Statistics, State of California Department of Public Health, 2151 Berkeley Way, Berkeley. This work was supported in part by Research Grant CH 00031, from the Division of Community Health Services, U.S. Public Health Service.

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Although no specific study has been made to affirm the accuracy of autopsy information reported on California's death certificates, numerous epidemiological studies have been made involving followback from death certificates to obtain additional diagnostic information from medical records, including autopsy protocols. An examination by the authors of several hundred completed schedules from one such study did not reveal any significant inaccuracy in recording autopsy performance on death certificates, nor has any investigator called attention to such a possibility.

### Autopsy Performance

The only published data on autopsy performance for the United States and other states is that of McMahan for 1955. At that time, 18 per cent of all death certificates in the United States reported autopsy. (The figure is undoubtedly higher since more than one-sixth of the death certificates furnished the National Vital Statistics Division for that year failed to indicate autopsy status.) In 1955, autopsy was done in about one-third of California deaths, a higher proportion than in any other state.

#### Autopsy Practices in California—1952 and 1962

In 1952, 108,660 deaths were reported in California; in 1962, 141,311. The number of autopsies performed in California during this same period rose from 32,469 to 52,736, an increase of 62 per cent. The proportion of deaths in which autopsy was done increased from 30 per cent of all deaths in 1952 to 37 per cent in 1962.

*County of Death and Certifier.* In all but six counties (Butte, Del Norte, Kings, Santa Barbara, Sierra and Tuolumne) ratio of autopsy to total deaths increased. Fifteen of the 17 metropolitan counties reported autopsy in more than 40 per cent of all deaths in 1962. San Francisco, at 57 per cent, was highest. Although 40 per cent of all California deaths occurred in Los Angeles County, autopsies were performed on only 29 per cent—the lowest proportion found in metropolitan counties.

Approximately one-fourth of all deaths were referred to coroners in both 1952 and 1962. Of these, the proportion in which autopsy was done rose from 58 to 64 per cent during this period. A decrease in the proportion of coroners' cases in which autopsy was done did occur in 13 California counties, the decrease exceeding 10 per cent in seven of the counties—Alameda, Butte, Contra Costa, Del Norte, Lassen, Sierra and Tu-

olumne. Although Los Angeles County ranked first and Alameda County third for numbers of deaths certified by coroners in 1962, the actual proportions in which autopsy was done declined: in Los Angeles from 43 to 38 per cent, in Alameda from 67 to 51 per cent. San Francisco and San Diego, ranking second and fourth, appreciably increased the proportions of cases certified by coroners which actually were autopsied. Most pronounced was the increase in the ratio of autopsies to coroner-certified deaths in Orange County from 29 per cent to 89 per cent. Considerable increase was also shown in the autopsy record of coroners in non-metropolitan areas, the proportion rising from 43 to 67 per cent of cases they certified.

Approximately three-fourths of all deaths in California in both 1952 and 1962 were certified by attending physicians. Permission to perform autopsy must be authorized by the closest legal next of kin of a deceased, and hence the proportions of physician-certified deaths which come to autopsy are considerably less than of those certified by coroners. From 1952 to 1962, the proportion of physician-certified deaths in which autopsy was done rose from 21 per cent to 28; metropolitan counties experienced an increase from 23 per cent to 30, nonmetropolitan counties from 11 per cent to 19. Six counties, again the more sparsely populated, did experience small decreases in autopsies in physician-certified cases, but elsewhere in California increases of 3 to 7 per cent occurred over the decade.

*Cause of Death.* With the exception of two conditions—emphysema and hypertension without mention of heart disease—the proportion of cases coming to autopsy increased for all of the 45 natural causes of death shown in Table 1 during the period in question. For emphysema, the large increase in numbers of deaths (259 to 1,706) may be a factor in the slight decrease in the proportion of deaths certified to this cause in which autopsy was done by both physicians and coroners. For hypertension without mention of heart disease, the number of deaths certified to this cause declined, and the proportion of autopsies in such cases declined slightly.

Attending physicians requested and secured permission for appreciably more autopsies in 1962 than in 1952 for many causes of death. Unquestionably, this contributed to more precise designation of cause of death. The proportion of permitted autopsies increased by 10 per cent or more







TABLE 2.—Deaths From All Causes and From Selected Chronic Diseases by Race, Sex and Age and Per Cent Autopsied California, 1962

Race, Sex and Age	All Causes		Cardiovascular- Renal Diseases (330-334, 400-468, 592-594)		Malignant Neoplasms (140-205)		Chronic Obstructive Respiratory Disease (502.0, 527.1, 241, 501, 502.1, 525, 526)		Cirrhosis of Liver (581)	
	Number	Per Cent Autopsied	Number	Per Cent Autopsied	Number	Per Cent Autopsied	Number	Per Cent Autopsied	Number	Per Cent Autopsied
Total .....	141,311	37.3	74,934	26.8	23,334	33.3	3,006	49.0	3,261	60.6
White, Male .....	74,788	41.8	39,336	32.2	11,670	37.7	2,098	46.3	1,900	62.1
Under 35.....	8,643	67.4	286	78.3	477	56.5	185	92.4	45	80.0
35-44.....	3,583	67.5	1,267	65.3	470	54.7	38	68.4	240	69.6
45-54.....	7,944	57.2	3,776	52.0	1,374	48.0	161	55.9	609	64.7
55-64.....	13,338	46.0	7,320	42.1	2,811	40.9	437	44.6	534	59.4
65 and over....	41,280	29.8	26,687	24.6	6,538	31.7	1,277	38.4	472	56.4
White, Female ....	57,295	29.7	31,777	19.3	10,260	27.8	711	51.2	1,131	58.2
Under 35.....	5,452	64.9	223	73.1	418	55.0	147	89.8	33	84.8
35-44.....	2,332	57.9	416	66.1	719	36.9	24	66.7	230	58.3
45-54.....	4,365	48.6	1,212	48.1	1,574	32.0	96	53.1	355	60.8
55-64.....	6,840	38.3	2,974	34.3	2,202	29.6	90	51.1	276	58.3
65 and over....	38,306	19.3	26,952	15.2	5,347	22.4	354	33.6	237	50.2
Negro, Male.....	3,992	57.1	1,482	42.2	580	47.4	88	76.1	107	59.8
Under 35.....	1,127	73.7	43	81.4	29	65.5	35	94.3	10	80.0
35-44.....	452	73.5	139	73.4	51	60.8	10	80.0	36	63.9
45-54.....	613	58.9	294	53.1	124	53.2	8	75.0	29	48.3
55-64.....	676	47.8	327	40.7	157	43.3	14	71.4	22	59.1
65 and over....	1,124	38.5	679	29.5	219	41.6	21	47.6	10	60.0
Negro, Female....	3,086	42.5	1,398	25.8	478	30.5	53	83.0	80	65.0
Under 35.....	778	72.8	48	75.0	35	57.1	32	100.0	13	84.6
35-44.....	271	56.1	87	49.4	64	31.2	4	50.0	23	69.6
45-54.....	414	44.2	181	37.6	104	31.7	5	60.0	28	57.1
55-64.....	531	33.7	324	30.2	111	22.5	4	75.0	8	50.0
65 and over....	1,092	21.3	758	15.2	164	29.3	8	50.0	8	62.5

Note: Numbers in parentheses are from International Statistical Classification of Diseases, Injuries and Causes of Death. Total figures include other non-white races.

Source: State of California, Department of Public Health, Death Records.

As might be expected, place of death perhaps more than cause of death or type of certifier influences decision to carry out autopsy. If a patient has been in hospital for a long period or several times before death, the need for autopsy may be less essential to affirm cause of death. Teaching institutions, however, have high rates of autopsy because of the obvious value in medical instruction.

Rates of performing autopsy among CVR deaths were about equal for deaths occurring in a facility (27 per cent) and those occurring elsewhere (25 per cent), the latter a reflection of coroners' autopsies in cases of sudden deaths. Autopsy was done in only 9 per cent of cancer deaths which did not occur in a facility. Autopsy rates for deaths occurring in nursing and convalescent homes, with their emphasis on pre-terminal care for the elderly, were low: 2 per cent of CVR deaths, 6 per cent of cancer deaths. By contrast, rates of autopsy in military and Veterans Administration hospitals and State university hospitals ranged between 64 and 75 per cent of deaths from CVR or cancer.

## Demographic Characteristics of Autopsy Cases

### Age-Sex Specific Autopsy Rates—1962

The percentages of persons dying reported as autopsy cases according to age and sex, for the white and Negro races, are shown in Table 2. For persons who died at ages under 35, rates of autopsy exceeded 64 per cent of deaths among white males and females and were above 72 per cent of deaths among Negro males and females. These figures reflect high autopsy rates for infants (more than 60 per cent for white and Negro males and females) and a higher proportion of coroners' cases—particularly accidental deaths—among the younger ages and in Negroes. Between ages 35 and 64, rates of autopsy dropped roughly 10 per cent of deaths for each ten-year age group among white males and females. Rates were lowest at ages 65 and over.

Autopsy rates for deaths from all causes were higher among males than females at all ages for both whites and Negroes. Sex differences were most pronounced in favor of males for Negroes at ages 35 and over.



Although the rate of autopsy for total deaths from cancer in California (33 per cent) exceeded that for total deaths from cardiovascular-renal diseases (27 per cent), this position was actually reversed for all ages under 65, where autopsy rates for CVR deaths equaled or exceeded those for cancer in all but one race-sex subset. Autopsy rates for CVR deaths exceeded 40 per cent among white and Negro males under 65, white females under 55, and Negro females under 45. Even higher autopsy rates were recorded for chronic obstructive respiratory diseases and cirrhosis of the liver.

#### Age-Sex Distribution of Deaths Compared to Autopsy Cases—1962

Chart 1 shows the age-sex pyramids\* for autopsy cases compared with deaths from all causes, cardiovascular-renal diseases and cancer for the white and Negro races. This graphic comparison of autopsy cases and deaths shows the degree to which autopsies are over- or underrepresented among deaths according to age and sex, a factor which may influence comparisons of age-sex specific mortality rates. Such a possibility for arteriosclerotic heart disease will be examined in the discussion which follows.

Age-sex pyramids for deaths from all causes show that white males were overrepresented in autopsy cases up to age 75, white females up to age 65. Both white males and females were considerably underrepresented in autopsy cases at ages 75 and over, females more than males. Underrepresentation began at earlier ages for Negroes: 55 for males, 45 for females.

The absolute differences between the percentages of deaths from all causes and autopsy cases were small for age groups under 75. With the

exceptions of white males aged 45-54, Negro males less than one year old and Negro females aged 65-74, these differences were less than 3 per cent. The relative differences in the percentages of deaths from all causes and autopsy cases, however, were large for most of the age groups. For example, males 35-44 constituted a percentage of white autopsy cases that was nearly twice as large as the percentage of males aged 35-44 among all deaths of white persons.

White and Negro males aged 35-64, who died of cardiovascular-renal diseases were overrepresented in autopsy cases to a greater degree than those who died of cancer. For cardiovascular-renal diseases, the absolute percentage differences favoring autopsy cases *vis-à-vis* deaths at ages 35-64 were about the same for white and Negro males (14 per cent against 13 per cent). The percentage of autopsy cases in this age-cause group was 1.8 times the percentage of deaths for white males and 1.5 times for Negro males.

White females who died of cancer were underrepresented in autopsy cases at ages 45 and over, and Negro females were underrepresented in autopsy cases at ages 35 and over.

#### Use of Autopsy Findings in Certifying Cause of Death

California is the only state which requests the certifying physician to report, when an autopsy was performed, whether the gross findings were used in determining the stated causes of death. The format shown below was adopted with the 1957 version of the California death certificate.

In 1962, where an autopsy was performed, the gross findings were reported used in determining the cause of death in 92 per cent of deaths certified by attending physicians and 99 per cent of deaths certified by coroners.

Examination of autopsy reporting on death certificates by underlying cause of death reveals some interesting facts. There were, for example, five causes of death for which 12 to 18 per cent of gross findings from autopsy were reported not used in determining the cause of death. These

\*The age-sex pyramid presents the age-sex distributions of populations in a condensed, visual form facilitating relative comparisons. The pyramid represents 100 per cent of a group. Males are shown on the left side of the center line; females are shown on the right. The vertical scale is divided into age groups, the youngest group at the bottom progressing to the eldest at the top. Percentages are placed on the horizontal line at the base so that comparisons can be made of the percentages that each specified age group constitutes of the total.

The type of graphic presentation used in Chart 1 combines the age-sex pyramids for deaths and autopsied cases into one figure. Two patterns are used, the one at the end of the bar indicates whether the percentage is higher for deaths or for autopsied cases. The percentages for deaths and for autopsied cases each add to 100 per cent.

### 33. AUTOPSY—CHECK ONE

- |   |  |  |
|---|--|--|
| <input type="checkbox"/> No autopsy performed | <input type="checkbox"/> Autopsy performed—gross findings used in determining above stated causes of death | <input type="checkbox"/> Autopsy performed—gross findings not used in determining above stated causes of death |
|---|--|--|

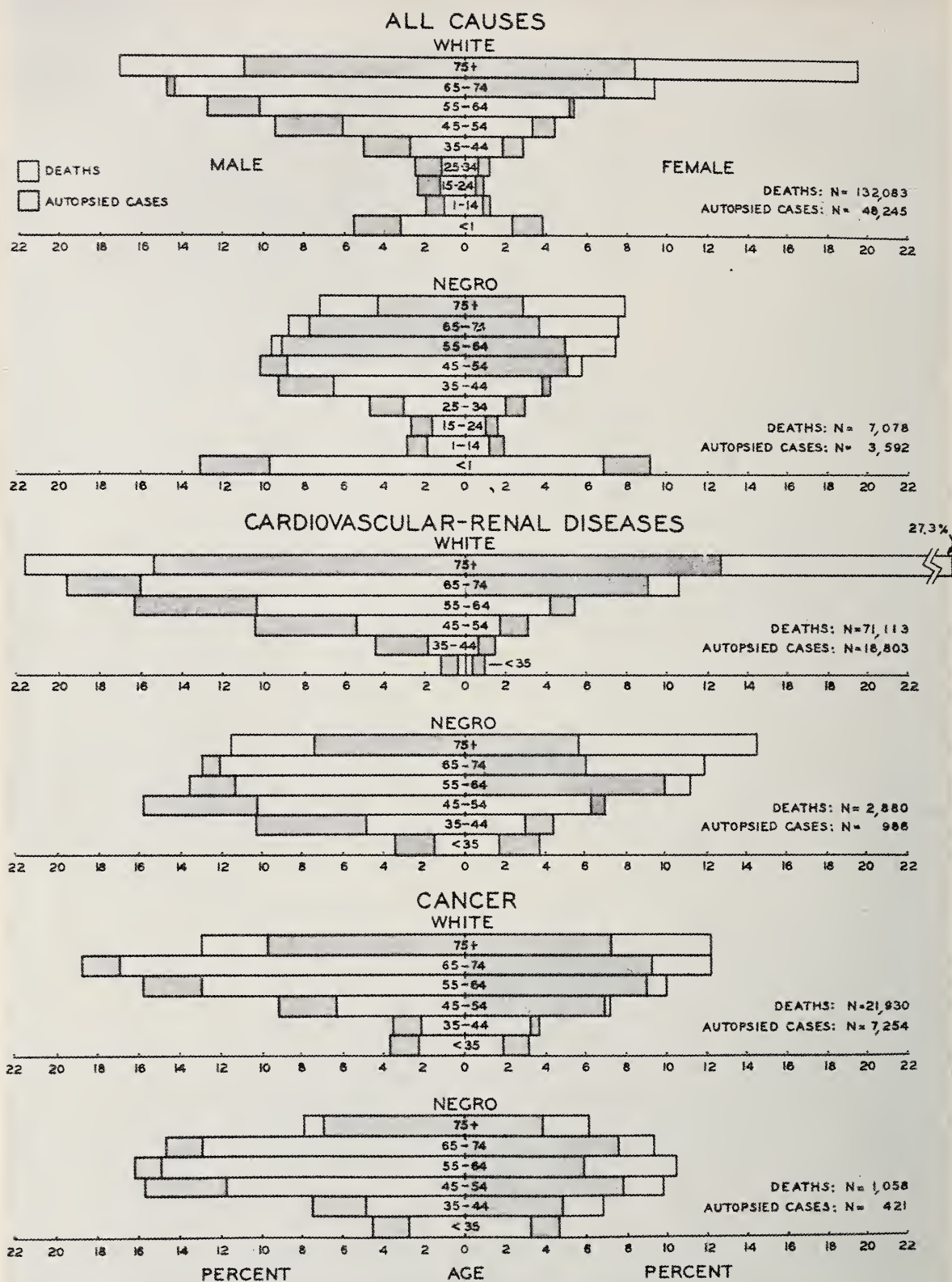


Chart 1.—Age-sex pyramids for deaths from all causes, cardiovascular-renal diseases and cancer compared with autopsied cases for the white and Negro races, California, 1962.



were cancer of the breast and cervix, Hodgkin's disease, leukemia and aleukemia and chronic nephritis. These diseases are usually diagnosed with confidence premortem. Also, gross findings were reported not used in determining the cause of death in 33 per cent of deaths coming to autopsy in hospitals associated with the State university, where there is likely to be a complete clinical work-up of patients.

Some of the above reporting may result from ambiguous interpretation of the words "used in determining." In the situation in which gross autopsy findings completely agreed with the clinically determined cause of death, the certifying physician might (1) check the right hand box because the stated cause of death was determined clinically and merely "confirmed" by autopsy or (2) check the middle box because, independent of the clinical diagnosis, gross autopsy findings "determined" the stated causes of death.

For some deaths where his clinical diagnosis is doubtful, the attending physician may request an autopsy, but the crucial evidence from autopsy may only be obtained from pathophysiological studies of tissues or organs removed from the body. These results may not be available at the time the certificate must be filed. In such cases, the certifying physician would presumably use his clinical diagnosis and check the right hand box. If later he found the diagnosis in error, he should use the amendment procedure to correct the death certificate.

In view of the possible ambiguities in the present autopsy statement, the need for a new statement with clearer definitions should be considered when the death certificate is revised in 1968.

#### **Amendment Procedure**

California's registration laws have historically provided a means whereby the certifying physician or coroner can amend the stated causes of death reported on the death certificate if autopsy results, particularly pathologic, toxicologic or microscopic findings, provide evidence that the original statement should be modified. Until recently, however, the legal procedure required that an affidavit by the medical attendant asserting that an error existed and showing the correct information, supported by an affidavit of another person having knowledge of the facts, be completed and sworn to in the presence of a notary public. This procedure has been little used. In 1960, only 344

affidavits were filed to correct the medical and health information on the 135,400 death certificates registered in that year.

In 1965, the California Legislature changed the provisions of the law relative to amendment of the medical and health data section of any record of death, fetal death or live birth. It is now possible for the certifying physician or coroner to correct a cause-of-death certification statement by stating the changes necessary to make the information correct on a simple record form, sign it and file it with the state or local registrar (see Public Health Report in *California Medicine*, November 1965). It is anticipated that the new, less cumbersome procedure will result in an increased number of corrections to original cause-of-death assignments.

#### **Discussion**

The organization of this data on California's autopsy performance and the characteristics of deaths in which autopsy was done have been made within the broader frame of studies which are being conducted to assess the accuracy of California's mortality statistics. Viewed in this context, California's overall autopsy performance is impressive. There is a much improved autopsy performance in the nonmetropolitan counties. If autopsy were done in deaths in Los Angeles County in the average ratio prevailing in the other metropolitan counties (45.8 per cent), the average for the state would be about 44 per cent.

The mortality patterns for cardiovascular-renal diseases, cancer, chronic obstructive respiratory diseases and cirrhosis of the liver are receiving increased attention by epidemiologists. Death rates for persons 35-64 years of age are of particular interest, since deaths under 35 are relatively few in number and beyond the age of 65 death is more likely to be the result of a disease complex than a single underlying cause. It is, therefore, reassuring to find the high ratio of autopsy in the "middle years" for these chronic diseases, especially in view of the fact that 39 per cent of all autopsy cases in 1962 were cases in which death occurred at ages 65 and over (20,651 out of 52,736).

The fact that autopsy cases represent a selected population is well known. Not all deaths, or even a random sample of deaths, go to autopsy. Rather, the choice of which deaths are to be autopsied is influenced by difficulties in ante-

mortem diagnosis, physicians' interest in particular cases or certain types of disease, attitudes of relatives and funeral directors, and legal requirements pertaining to certain types of death.

The risk of deriving fallacious conclusions when using an autopsy series to study disease incidence, etiology and the relationships between diseases has been described by Mainland.<sup>4</sup> The possible biasing effect of autopsy reports on community mortality statistics has not received much attention, however. Specifically, the question raised is, does the number of autopsies performed affect reported trends and differentials in mortality among various subgroups of the total population of deaths?

The age-sex pyramids for California show considerable over- and underrepresentation of autopsy cases compared with total deaths. This fact by itself is not so important with respect to mortality rates unless the use of autopsy data has the systematic effect of increasing the proportion of deaths attributed to one specific disease rather than another. Several investigators have shown that autopsy does have this effect for coronary artery disease.<sup>1,3,6,7</sup> A comparison of clinical and pathological findings by Paton revealed that less than one-half of the myocardial infarcts demonstrated at autopsy had been detected premortem.<sup>6</sup>

Since in California there was a recorded reduction in mortality from arteriosclerotic heart disease including coronary disease (ISC\* 420) among the white male population ages 35-64, between 1950 and 1960, whereas the United States data indicated an increase in mortality in this age-sex-race subset, the possible biasing effect of autopsy performance on these results should be considered.<sup>2</sup> The available facts are these:

1. California has very high autopsy rates for total cardiovascular-renal diseases in the "middle years," 35-64, for white males (see Table 2). The autopsy rates for arteriosclerotic heart disease including coronary disease are almost identical to all CVR diseases in the three ten-year age groups.

2. These autopsy rates are higher than the rates for the nation as a whole. How much higher is unknown, but the ratio is probably as high as two to one, judging from McMahan's data.

3. California's autopsy rates for cardiovascular-renal diseases have increased from 21 per cent to 27 per cent during the past decade. The national rates have probably increased also, but the rela-

tionship between them has probably not changed much.

4. In the California white population who died of cardiovascular-renal diseases, males aged 35-64 were represented 14 per cent more in autopsied cases (31 per cent) than in total deaths (17 per cent). The percentage of autopsy cases was 1.8 times the percentage of deaths in this age-sex-race cause group.

5. The care with which coroners investigate cases of sudden death can substantially affect mortality statistics for coronary disease (ISC 420.1). California's coroners are autopsying 52 per cent of all deaths from cardiovascular-renal diseases and 73 per cent of deaths from heart disease specified as involving coronary arteries.

6. Studies cited above have shown that the use of autopsy data increases the proportion of heart disease deaths attributed to arteriosclerotic heart disease.

7. There is evidence from the death certificate that the gross findings from autopsy are generally considered in California in making the determination of causes of death.

These facts suggest that California is finding more "true" arteriosclerotic heart disease deaths in the white male population aged 35-64 than is being found in the United States generally. Yet despite this "diagnostic assist" the reported death rate for California has declined.<sup>†</sup>

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\*International Statistical Classification of Disease, Injuries and Causes of Death, published by the World Health Organization.

†Another factor which could account for the reported difference in mortality trends for arteriosclerotic heart disease in California and in the United States is a change in the manner of reporting the components of cardiovascular-renal diseases on death certificates. This possibility is being investigated for the California data.



# Hemorrhage During Long-Term Anticoagulant Drug Therapy

## Part V. Unusual Bleeding Episodes

JOHN MARTIN ASKEY, M.D., *Los Angeles*

BLEEDING is the most important drawback to long-term anticoagulant therapy with the coumarin drugs. Most episodes are minor, but some prove serious or even fatal. Despite ordinary care in the selection and management of the patient, bleeding may still occur in unpredictable circumstances. It is often the result of composite errors in management. Together with the physician, the patient and the laboratory, the pharmacist has emerged as an important member of the therapeutic team.

The following cases should provide pointers in preventing future episodes of a similar nature. They emphasize the need for *extraordinary* care of the patient who is receiving long-term anticoagulant drug therapy.

### Reports of Cases

Failure to verify a telephoned prescription led to an error in the following case:

CASE 1. A 64-year-old woman with longstanding Parkinson's disease had taken Kemadrin® (procyclidine hydrochloride) three times daily for several years. When she traveled to Los Angeles to visit her family, she discovered her supply of tablets had been left behind. Rather than locate a new physician, she requested that the family dentist call a pharmacy for a new supply of 5 mg Kemadrin® tablets. The prescription was filled but the bottle was not labeled. Several weeks later, the patient noted large, ecchymotic areas on her body, oral bleeding and hematuria. The tremor and rigidity of Parkinson's disease had worsened

and she was growing weaker. On hospital admission, pronounced hypoprothrombinemia was noted. Because there were no definitely incriminating data, the diagnosis of hypoprothrombinemia (either idiopathic or possibly secondary to carcinoma of the liver) was made. All medication was stopped and vitamin K1 was given. The ecchymosis and hematuria disappeared and the patient was discharged and allowed to resume taking her supposed Kemadrin® tablets. Ten days later, ecchymosis and hematuria returned. The patient's son, a lay science editor, found that in having the supposed Kemadrin® prescription filled, the telephoned prescription had been transcribed by the pharmacist as "Coumadin®"; the patient had been taking 5 mg of Coumadin® (warfarin-sodium) three times daily. Discontinuance of the anticoagulant drug cleared the hemorrhagic symptoms.

*Comment:* In telephoning the prescription for Kemadrin®, there was no verification by spelling back the name and restating the dosage. The unfortunate similarity, not only of the name but size of the dose, contributed to the error. Moreover, the name and dose of the drug were not marked on the label. Had this been done, the patient or her son would immediately have detected the error. This case is probably the result of composite errors in management by the patient and by the pharmacist, and also by her personal physician for not stressing to her that only a physician should reorder the drug.

The mutual responsibility of physician and pharmacist in assuring that a coumarin drug is not mistakenly administered for another, or that a more potent coumarin drug is not substituted for

This is the final article in a series of five on Hemorrhage During Long-Term Anticoagulant Drug Therapy.

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one of lesser potency, is emphasized in other reports. Donald and associates<sup>1</sup> reported that a pharmacist, in error, filled a prescription for Tromexan (ethyl biscoumacetate) with Dicumarol® (bishydroxycoumarin). Fisher<sup>2</sup> mentioned a fatal episode of cerebral hemorrhage following the administration of 75 mg of Coumadin® instead of Dicumarol®. Cerebral hemorrhage has occurred when the labels on digitalis and Dicumarol® bottles unaccountably became switched. The anticoagulant drug was supposedly discontinued when bleeding occurred but actually was continued due to the alleged mislabeling.

The pharmacist may be led into error by the patient, as in the following case:

CASE 2. A 55-year-old Los Angeles woman had mitral stenosis, controlled atrial fibrillation and embolism controlled by long-term antithrombotic drug therapy (Dicumarol®). She had been under treatment for three years, taking one 25 mg tablet daily with no hemorrhagic complications. She planned to take a 10-day trip by riverboat from Cincinnati to New Orleans and back. In Cincinnati, she discovered she had left at home her Dicumarol® and the card giving the daily dose. Since there was not time to consult a physician, she located a pharmacist, told him her plight and the necessity for the daily Dicumarol®. Although the bottle at home was properly labeled, and she knew she took one tablet a day, she did not know the size of the tablet. The pharmacist said that in this emergency he would accommodate her if she could pick out the tablet. She chose the 50 mg tablet instead of the 25 mg, and for three weeks she took twice the usual dose. When she returned to Cincinnati, she had diffuse ecchymosis, a subconjunctival hemorrhage and bloody urine. She immediately flew home. Her prothrombin time was found to be over 60 seconds. The disorder responded to vitamin K1 administration and the temporary discontinuance of Dicumarol®.

*Comment:* This was a result of errors by both the patient and the pharmacist. Even though the patient was instructed always to consult a physician if problems arose when traveling, unforeseeable circumstances prevented her doing so. Furthermore, she did not know her exact dose and did not think of verifying it by long distance telephone and her physician had not thought to so instruct her.

The following case illustrates the failure of a patient to assume his responsibilities in anticoagulant drug therapy.

CASE 3. A 72-year-old dental surgeon had been taking an antithrombotic drug (Dicumarol®) for seven years following myocardial infarction. He was under constant supervision in Kansas City but did not consult a physician as instructed when he moved to Los Angeles. He continued obtaining the drug through his brother-in-law, a pharmacist in Kansas City, who believed the patient was still under a physician's care. After a year, massive ecchymotic areas developed all over his body. The prothrombin time was 60 seconds. Fortunately, there was no internal bleeding and the ecchymosis gradually cleared after Vitamin K1 was given.

*Comment:* This case is due to patient irresponsibility. Such failure by a patient to follow instructions is either due to low intelligence or to foolhardiness. Most patients are aware that bleeding episodes may result during anticoagulant therapy (and probably will, if treatment is continued long enough) but also understand that these will be minor and certainly acceptable in light of the antithrombotic protection.

In some instances bleeding actually proves to be a life-saving signal of early cancer.<sup>3,6-8,10,11</sup> The following case illustrates this point:

CASE 4. On the advice of a neurologist, an 85-year-old woman had taken Dicumarol® for two years for progressive carotid artery insufficiency. Her prothrombin time had been maintained between 20 and 30 seconds (control 14 seconds). One day she noted slight vaginal bleeding, and pelvic examination showed the uterus to be twice normal size, although the cervix appeared normal. Dilatation and curettage obtained granular necrotic material mixed with blood clots. The material was identified as from "mixed mesodermal sarcoma of the uterus." She was treated with radium, followed later by external irradiation. Four years later, she was still in good health.

*Comment:* Apparently a pelvic examination was not done in this patient until after the bleeding occurred. This is a common oversight in long-term anticoagulant drug therapy. Another preliminary study frequently not done is a proctoscopic examination. This is considered a routine part of the periodic physical examination but often is omitted before long-term anticoagulant drug treatment. If



gross rectal bleeding occurs, the examination should not be limited to proctoscopy but should include a barium enema study to rule out carcinoma of the large bowel.

Although in certain circumstances a healed peptic ulcer does not contraindicate treatment, a history of an old ulcer demands intensified surveillance, while recognition of an active ulcer ordinarily precludes treatment. A history suggesting an ulcer ordinarily makes roentgen examination and stool studies for blood mandatory. Thorough eval-

uation of the patient before anticoagulant drug therapy is begun should reduce the number of hemorrhages occurring unexpectedly with the prothrombin level within supposed "therapeutic range."

## Discussion

Oliver Wendell Holmes said, "It is often more important to emphasize the obvious than attempt to elucidate the obscure." Physicians can prevent many of the hemorrhagic episodes that occur during long-term anticoagulant drug therapy by some fairly obvious but still important precautions. The hemorrhages reported here were, in retrospect, preventable—and they could have been fatal had a serious latent lesion been present.

Careful selection of only those patients who can be relied upon to follow directions rigidly is still fundamental, of course, but the physician in giving his directions must caution against the unusual as well as the more obvious circumstances that may induce bleeding.

Unusual situations may call for all the ingenuity of a sleuth.<sup>10</sup> Unsuspected, surreptitious self-administration of an anticoagulant drug over a long period may produce puzzling clinical bleeding. O'Reilly, Aggeler and Gibbs<sup>9</sup> cited the example of a nurse who denied taking Dicumarol<sup>®</sup> although the drug was subsequently detected and measured chemically in her plasma. They noted that the nine previously reported instances of factitious bleeding were all in persons associated with the medical profession (eight nurses, one physician) and emphasized the need to suspect self-administration of a coumarin drug whenever hemorrhagic symptoms appear in medical personnel in association with low prothrombin complex activity. Marlowe<sup>4</sup> is preparing a report on a non-professional who surreptitiously diverted her husband's coumarin drug to herself and had diffuse hematoma and bilateral kidney disease.

Meyer<sup>5</sup> described an unusual experience in the early days of testing the drug which, he said, "in retrospect seems humorous but was not so funny at the time and it might well have been tragic." Two patients with the same name were in the same hospital ward at the same time. While one received Cumopyran (cyclocumarol), prothrombin time determinations were carried out daily on the blood of the other. Since the former patient seemed resistant to the drug, the dosage was progressively

### RULES TO PREVENT ERRORS WITH ANTICOAGULANTS

The physician must emphasize the detailed safeguards essential to the delicate liaison between physician, patient and pharmacist. This can best be done by:

1. Giving the patient a written list or a card of instructions and some vitamin K1 for use in case of injury.\* Since the card may be mislaid, the patient must know the daily dose of the specific drug in milligrams (Case 2).

2. Emphasizing the need to consult a physician if problems arise while traveling, as well as the need for periodic determination of prothrombin time. If the patient hesitates to consult an unknown physician, he can always telephone his personal physician long-distance (Case 2).

3. Following up all patients who have moved to ensure that they continue under a physician's direction (Case 3). It may be necessary to telephone or write the patient, but the physician must satisfy himself that the patient is still under medical care. Abrupt discontinuance of the drug is just as undesirable as unsupervised continuance.

4. Printing the name and dose of the drug on a prescription blank, instructing that the name and dosage of the drug be shown on the label and specifying "no refills" unless for a select, trustworthy patient.

5. Avoiding telephone prescriptions except when circumstances make it mandatory, and then spelling out the drug name and having the druggist repeat it distinctly (Case 1).

6. Meticulous inquiry regarding potential gastrointestinal lesions, and x-ray examinations if the history is suspicious.

7. Routine pelvic, proctoscopic and stool examinations before treatment.

\*We are now adding wrist tags in certain instances. The tag reads "Taking anticoagulants. See card in wallet." (Medic Alert Foundation, Turlock, California.)

increased. The error was realized when subcutaneous bleeding developed at the site of the hypodermoclysis needle puncture.

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#### Generic and Trade Names of Drugs.

Procyclidine hydrochloride—*Kemadrin*.

Warfarin-sodium—*Coumadin*.

Ethyl biscoumacetate—*Tromexan*.

Bishydroxycoumarin—*Dicumarol*.

Cyclocumarol—*Cumopyran*.

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# *For Affliction Does Not Come From the Dust*

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ON THE EARLY MORNING of a spring day, a few years ago, I stood on the rim of a hill in the wastelands of the West, watching with interest the results of man's technical invasion of the desert valley below. Among my companions on this occasion was an American of national stature and recognition. In spite of the apparent age-old serenity of our surroundings, an undercurrent of excitement prevailed, and men spoke in the hushed tones of those who tread on the thresholds of cathedrals. On radio command, the panoramic desert scene was cut out by the blackness of dark glasses and even the brightness of the sun paled to that of a wan moon, dimmed by summer haze. There commenced then, over the loudspeaker a metronomic counting cutting through the cool morning air with the precision of a clock ticking off the seconds of doom, nine—eight—seven—six—five—four—three—two—one, and then, the blinding flash of nuclear fission.

The currents of brilliant colors in the swirling fireball, like some gaseous whirlpool of Dante's *Inferno*, had barely subsided when I turned to observe the reaction of my scientific companion, who was witnessing his first atomic explosion. He stood, dark glasses in hand, with tears coursing down his cheeks, unchecked and unnoticed, oblivious of his immediate surroundings, staring at the evidence of this unleashed power rising like some great genie over the sandflat below.

That night, over the evening meal, in a Las

Vegas restaurant, my companion apologized for his apparent display of emotions, stating that at the time he had been unaware of any objective evidence of his deep subjective reaction. He continued to explain that the morning's demonstration of man's ingenuity in wresting from Nature this particular secret of material power had overwhelmed his sense of personal and national accountability. It was his considered judgment that our scientific achievement posed a dire threat to mankind unless related to moral responsibility.

"We dare not forget," he emphasized, "that man is his brother's keeper."

Our world is faced with an explosive expansion in the field of science. Scientific information is said to have doubled in the first half of this century and then doubled again in the past 10 years. Ninety per cent of all scientists are *living today*. Our scope of interest knows no bounds and reaches from the searching eye of the electron microscope, dissecting as it does the minutest components of the single living cell, to exploration of the galaxies in space, millions of light years removed. Yet in spite of so bountiful a harvest of scientific knowledge, an uneasiness pervades the mind of thinking man. Although our globe now is encircled in a matter of a couple of hours, this same globe is divided into distrusting power-camps, each guarding its own physical and ideological perimeters with material weapons capable of destroying the very globe itself.

It is in this context of uneasy mind that Rene Dubos,<sup>5</sup> professor at the Rockefeller Institute, writes:

"There is no longer any thoughtful person who believes that the conversion of Science into more

EDITOR'S NOTE: This article is published not only for the quality of the thoughts it expresses but in recognition of the increasing emphasis, both in medical organizations and teaching institutions, on the interrelationships of medicine and religion.

Address at the installation of Granger E. Westberg as the first Dean of the Institute of Religion, Texas Medical Center, Houston, Texas, 2 April 1965.

Submitted 14 June 1965.

Power, more Wealth, or more Drugs, necessarily adds to health and happiness, or improves the human condition. Indeed, haphazard scientific technology pursued without regard for its relevance to the meaning of human life, could spell the end of civilization."

The travail of those who observe the gradual erosion of personal identity in the strong tides of scientific progress, is expressed in the words of Kenneth Boulding<sup>2</sup>: "Science might almost be defined as the process of substituting unimportant questions which can be answered for more important questions which cannot."

There is not the least intention here to derogate science but rather to emphasize the dignity of man as a person and to appeal for a growth in symmetry of the individual. Science must and will continue her advance, ever pushing back the frontiers of the unknown, and yet at all times must remain the servant of man, *not* his master. The mere possession of facts or techniques or knowledge, in no wise guarantees a satisfactory answer to the pressing problems confronting our daily lives. The distinction between knowledge and wisdom is not merely an exercise in theoretical semantics, but actually is the very issue upon which personal values will be determined. William Cowper,<sup>4</sup> with poetic instinct, focused clearly on this critical matter in the following lines:

Knowledge and wisdom, far from being one,  
Have oft times no connexion. Knowledge dwells  
In heads replete with thoughts of other men;  
Wisdom, in minds attentive to their own.  
Knowledge, a rude unprofitable mass  
The mere materials with which wisdom builds,  
Till smooth'd and squar'd and fitted in its place  
Does but encumber whom it seems T'enrich.  
Knowledge is proud that it has learned so much,  
Wisdom is humble that he knows no more.

Medicine may be found in the vanguard of scientific exploration, constantly seeking to unravel the secrets of birth, health, disease and death; and then, with equal diligence applying these hard-earned discoveries in the ceaseless combat for the preservation of man's health and the prolongation of his fruitful years. With the ravages of infectious diseases in great part subdued, the battle lines now are being drawn in confrontation with the degenerative and neoplastic diseases prevalent in the older age population. This very change in tactics is evidence of the success of previous campaigns which have permitted man to mature safely through younger age groups whose ranks in the

quite recent past were decimated by the ravages of epidemic disease.

It is not a purpose of this presentation to dwell on the miracles of modern medicine, for the public today is confronted daily with convincing evidence of medical progress. This very progress, however, poses a certain threat to the symmetry of the treatment of man as a whole being. Dr. William Stahl,<sup>8</sup> director of surgical research at the University of Vermont College of Medicine, recently wrote:

"Much of the advanced knowledge gained about patient care and the treatment of disease must be mediated through or monitored by a plethora of mechanical devices. Certainly one who has seen procedures such as open heart surgery, artificial kidney dialysis, organ transplantation, hypothermia and hyperbaric or high pressure oxygen therapy, is sometimes at a loss to find the *patient* amidst the welter of monitoring devices, electrodes, catheters, pressure recorders and blinking lights."

Specialization in medicine was inevitable when the horizon of medical knowledge became too broad for the comprehension of one person. As time moves on, this tendency will increase with a continued fractionation of the broad spectrum of medical disciplines. Certainly this changing pattern makes available highly specialized and efficient techniques of medical diagnosis and therapy, but all too frequently, the focus of attention narrows upon a *fragment* of the whole person. No one bemoans the passing of the horse and buggy doctor with his well-intentioned but far too often inadequate therapeutic and prophylactic efforts, and yet, this dignified and respected man of medicine dispensed a compassion of human understanding so essential to the healing of the whole body. Too often today we find this compassion lacking in the technically efficient but impersonal mechanics of modern medicine.

The practice of medicine is a fused product brought about by the ingenious blending of two elements, each necessary in the successful application of the profession to its mission of healing. The science of medicine on the one hand, is that broad stream swollen by the many factual tributaries from which those possessing the necessary intellectual receptacles may dip to slake their thirst for knowledge. This essential component is never lost with the death of the contributors but lives on to water and give growth to those who follow in their footsteps. Successors in medicine



build on the scientific discoveries of those who pioneered. Sir Alexander Fleming poured into the stream of medical science his great contribution and others have watered the original frail seed of antibiotic therapy until it has grown into a tree whose branches and roots now encompass a vast area in the field of therapeutics.

The other fraction of this effort might be designated as the *art* of medicine, a fraction which during the past decades has been crowded into a role of less and less participation. This element pertains to the personal application of the science of medicine and that delicate, but so important, reaction brought into play by the physician-patient relationship; and, in contra-distinction to the *science* of medicine, the *art* cannot be passed on accumulatively from generation to generation. Rather, it must be learned anew by each neophyte of the medical profession. Just as the great artist carries with him to his grave the genius of those masterful strokes of brush on canvas, so is the art of medicine enfolded in the shrouds of the physician.

The distinguished Swiss physician, Paul Tournier,<sup>10</sup> in exploring the person of man, wrote:

"Information is intellectual, whereas communion is spiritual; but information was the path that led to communion. Information speaks of personages. Communion touches the person. Through information I can understand a case; only through communion shall I be able to understand a person. Men expect of us that we should understand them as cases; but they also want to be understood as persons. There are two routes to be followed in the knowledge of man: one, is *objective* and scientific, the other, is *subjective* and intuitive. They cannot be equated together, for they require the exercise of utterly different faculties. One proceeds by logical analysis and precise assessment; the other by a total understanding. One is an endless progression; the other is a sudden and complete discovery."

The wise physician is aware of that mysterious triad fusing man into a single being which Holy Writ informs us was created in the image of God, and the perceptive physician visions health in its broadest concept, to encompass the body, the mind and the spirit. To heal the body in the face of a broken mind or spirit is but a partial victory, and one which all too frequently reverts to failure initiated by the inroads of mental or spiritual disease on the physical component. The past few decades have had much to say about psychoso-

matic medicine, and current medical thinking emphasizes the effects of man's mental and spiritual status upon his physical wellbeing.

Dr. Paul Tillich,<sup>9</sup> the eminent theologian, in his book on healing, wrote:

"Jesus was called a physician, and it is the physician for whom we ask first when we are looking for health. And this is good. For, as all generations knew, there is healing power in nature. And much healing is possible if this power is wisely used and skillfully aided. Those who despise this aid and rely on the power of their will ignore both the destructive might and the constructive friendliness of Nature . . . the physician can help, he can keep us alive, but can he make us whole? Can he give us salvation? Certainly not, if discord, cleavage, restlessness rule our mental life, if there is no unity and therefore no freedom in our soul, if we are possessed by disordered anxiety and disordered aggression, if mental disorder or disease are threatening or have conquered us."

Eliphaz, the Temanite,<sup>1</sup> although he demonstrated in his discussions with Job an inadequate equipment for the ministry of consolation, *did* utter a profound truth when he stated: "For affliction does not come from the dust, nor does trouble sprout from the ground, but man is born to trouble as the sparks fly upward." What he would appear to mean here is that affliction does not just happen, and is not related merely to the material facet of man, but rather is the result of a complexity involving the spiritual and mental as well as the physical components.

The physician of today, resplendently equipped as he is with the accoutrements of medical science, nevertheless appreciates his limitations in the face of the mystical nature of man and realizes that the material or physical master key alone cannot unlock all of the storehouses of health. He humbly acknowledges that the clinical laboratory while competent to assay the physiological status of his patient, is not equipped to assess a level of spiritual wellbeing.

During the Second World War, I served for a time with a roving band of guerrillas behind enemy lines. My interpreter, a Communist physician, and I, had ample opportunity for protracted discussions as we hid in caves or camped in the mountains between periodic military forays. In debates in which we set forth or defended our individual philosophies of life, my materialistic friend would express repeatedly his amazement that I, a

man of science, could believe in anything that could not be demonstrated by scientific standards of proof. He prided himself in his staunch belief only in those things which could be tested in the exacting crucible of laboratory research or solved by the precise intricacies of a mathematical formula.

One sunny afternoon as our motley band of warriors rested on the side of a mountain, my interpreter physician informed me that we had been surrounded by the enemy and our position was most precarious. Plans called for an attempted dash through this encirclement after dark. Letters home might be written and hidden safely where they might be recovered later and forwarded to loved ones in the event of death.

As I sat writing a farewell letter to my wife and children, each breath of air, each glint of sunlight on the sparkling mountain stream, each copper-tinted autumn leaf, each cascading warble of the birds, each sigh of the wind became crystallized into something a thousand times more beautiful and sweet when viewed in the perspective of life and death. My Communist friend sat a stone's throw away, deeply engrossed in the bitter-sweet task of composing words which might be a final communication with his wife and children.

In the midst of writing I paused to interrupt my companion's sober reflections and to question him as to whether the significant thoughts embodied in his composition were such as could be proved in the test tube or on the blackboard. His answer was an averted look, for he knew as well as I did that our most profound thoughts in the face of the impending crisis were not related to the material things of life, nor could they be measured by the tools of physical exploration. There were neither qualitative nor quantitative tests that could evaluate accurately our intimate personal experiences of love or hope.

In a brief and inadequate form we have recognized the scientific progress of this century and at the same time evidenced an uneasiness lest medicine, wrapped in the fascination of a deluge of brilliant discoveries, forget that "affliction does not come from the dust" and lose sight of the fact that man is a person whose substance is far greater than the sum of his components. It is quite natural at this point that we turn our attention to the historical and significant part in the care of the sick played by our professional brethren of the cloth.

In the earliest recorded histories of man the

roles of the priest and the physician have been so closely related as almost to be inseparable. Priests of old were the intellectuals of their time and in this capacity they observed, recorded, and stored the medical knowledge of the day. King Ashurbanipal of Assyria, during the seventh century before Christ, collected some 800 clay tablets relating to medical matters and placed them in the great library of Nineveh. This association of the priest and the physician is noted historically through the centuries in the writings of Egyptian medicine, the Vedantic medicine of India, the Zoroastrian medicine of Persia and the Mosaic medicine of the Children of Israel. Calder,<sup>3</sup> in tracing the early history of medicine, wrote:

"Moses, as the adopted son of Pharaoh's daughter, was in all probability, trained for the priesthood, and so acquired a knowledge of hygiene and medicine. His religion—the Monotheism of the Jews—did not accept the Gods of disease and healing, nor the exorcism, nor the astrology, nor the incantations—the priests were not physicians but medical officers of health. They were remarkably aware of communicable disease. The Book of Leviticus is an excellent sanitary code, giving instructions on proper and improper food; clean and unclean objects; the hygiene of childbirth and menstruation; and the prevention of contagion. The transmission of leprosy was recognized and directions were given for the isolation of people with infections and for the disinfection of their property."

Through the pages of the sacred books of the Hebrews and the Christians one observes a growing importance of the person of man. Christ's admonition that thou shouldst love thy neighbor as thyself and the clarifying parable of the Good Samaritan placed a new dimension on the measure of man, a physical or natural factor as well as a spiritual. Just as the physician in his modern environment of surging scientific progress must be aware of the importance of the spiritual in the etiology and therapy of disease, equally important is the need for a deeper appreciation on the part of the clergy of the significant role man's physical nature plays in his spiritual welfare. Albert Schweitzer<sup>7</sup> expressed this thought as follows:

"All spiritual life meets us within natural life. Reverence for life, therefore, is applied to natural life and spiritual life alike. In the parable of Jesus, the Shepherd saves not merely the soul of the lost sheep but the whole animal. The stronger the rev-



erence for natural life, the stronger grows also that for spiritual life."

It was because of this very reverence for physical life that the Christian Church played so significant a role in the development of hospitals for the care of the sick.

The purpose of this particular conclave, meeting as we are today, surrounded by towering evidence of scientific medical achievement, is to inaugurate Dr. Granger E. Westberg as the Dean of the Institute of Religion. And what is this Institute of Religion? It may be defined by a quotation taken directly from an official brochure of information:

"The Institute of Religion, in the Texas Medical Center, Houston, is a pioneering program in the field of health. It joins the findings of medicine and the insights of religion in healing. Instruction and inspiration are offered to the entire health team of physicians, nurses, ministers and medical students.

"It is the first institution of this kind in any medical center in the United States. The program embodies the experience of nearly four decades of clinical training. Medical and nursing professionals deepen their insights into the meaning of religion and health and the place of the clergy in healing. Ministers learn pastoral care in a life situation, under competent supervisors. The goal is to develop a team approach to spiritual problems in the field of health."

The concept of a team approach, namely, the physician and the priest, in the care of man's illness is as ancient as the history of man himself; and yet it is only within recent times that a serious and concerted effort of joint education and joint participation in this particular facet of health care has become evident. The leaven of interest appears to be working in both professional camps. The pioneering efforts of the Institute of Religion, here in the Texas Medical Center, have crossed not only state and national boundaries but intercontinental boundaries as well.

The American Medical Association demonstrated a very real interest in the closer physician-clergyman relationship in patient care by the establishment in 1961 of a Department of Medicine and Religion. This department, at present directed by the Reverend Dr. Paul B. McCleave, has fostered cooperative physician-clergy programs in an increasing number of medical societies the length and breadth of the nation.

When I served as dean of St. Louis University School of Medicine it was my responsibility to deliver a series of lectures to the senior medical students on a variety of practical as well as philosophical subjects best summarized under the general heading "The Art of Medicine." Parenthetically, the appointment of a Presbyterian as the dean of a Jesuit School of Medicine was an ecumenical act of rather unusual dimensions—and this before the official actions of the beloved late Pope John. One of the subjects in this series of presentations dealt with the relationship of the physician to the clergyman, the priest or the rabbi in the care of the patient, and pointed out that in a team approach to any situation the areas of responsibility of the individual units of the team should be defined clearly. In a well coordinated action each member has a contribution to make, a contribution based on a background of wisdom acquired through a period of rigorous education and maturation.

In a health team, problems of incoordination will arise—and this often to the detriment of the patient—when a member of a team begins to act authoritatively on the fringes of his particular area of competence. Thus, the clergyman, untrained in psychiatry, who attempts to encroach upon this specialized field becomes a cause for concern. Similarly, the physician, untrained in theology, who would don the cloth of the clergy and make decisions on the theological fringes of medical science, is practicing without proper qualifications. This definition of specific areas of responsibility does not preclude the physician's interest in the spiritual welfare of the patient nor the clergy's concern in the parishioner's physical wellbeing. The witness of a physician with religious faith can play a significant role in the solution of a patient's spiritual problem and in this capacity he assists, not primarily as a physician, but as a man of religious understanding and on the basis of their common humanity. By the same token, the clergyman, priest or rabbi, educated in an institution such as this, which we honor by our presence here today, carries with him insight into the physical, mental and spiritual problems of the sick which immeasurably enhances his services as a shepherd to his pastoral flock.

Dean Westberg, to direct the destiny of this institution is a most peculiar honor as well as a wonderful responsibility. May the Institute of Religion under your guidance continue her research in join-

ing the findings of medicine and the insights of religion for the benefit of the suffering. May your efforts focus on the better appreciation, by clergyman and physician alike, of a balanced order of health values by virtue of a clearer interpretation of the whole of man's life.

Many centuries ago a Persian poet,<sup>6</sup> with remarkable insight into the physical and spiritual components of man, wrote:

*"Shouldst thou repair, then, to thy larder  
and there, find of all thy once bounteous store,  
but two loaves remain, I yet council thee to  
sell ONE wherewith to buy white hyacinths to  
feed thy soul."*

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# Current Status of Heart Replacement

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■ *A review of heart replacement involves discussion of the artificial heart and the cardiac homograft. The mechanical substitute shows destruction of blood cellular elements and clot formation, regardless of the type of pump used. Significant postoperative survival remains as the major goal. Animals having homograft substitutions show prolonged survival and good cardiac function. Philosophical and legal problems rank above the rejection phenomenon in curtailing clinical isotopic replacement.*

ENDEAVORING for many years to perfect methods for total or partial cardiac replacement, researchers now well realize that in most instances only the most superficial considerations have been encountered. It is apparent that the more detailed problems of this major project remain to be answered. When these ideas come forth, ensuing clinical substitution of the heart will represent not only the culmination of one of man's greatest research efforts, but also the realization of one of his age-old dreams.

As in all fields of major research, many methods of cardiac replacement have been described and tested. Similarities are striking in the ultimate design, and especially in the problems resulting from these various techniques. From the standpoint of discussion these projects must be placed under two distinct headings, the artificial and the homograft.

## Artificial Heart

The first serious interest in an artificial heart came in 1956, and then in a flurry many styles of pumps were built, developed and tested. Although there are eight basic designs of pumps and three usable means of propulsion—electrical, hydraulic

and skeletal—most of the problems are common to all. Regardless of the material from which the artificial heart is constructed or of mechanical factors or propellants, it should be judged on its relationship with the host.

Major difficulties in this relationship over the entire history of these projects continue to be the following: complex and bizarre blood destruction and clotting, absence of reflex control of the artificial organ by the host, the presence of a foreign body, and significant fatigue of the materials in moving portions of the pumps. Problems of joining synthetic to living tissues, although improved recently, still are great.

Using two supposedly atraumatic pumping mechanisms, the roller pump and the ventricle type pump, to perfuse animals for 16 to 40 hours, Kusserow<sup>13</sup> described, sequentially, the resulting changes: (1) rapid destruction of some red cells with appearance of free plasma hemoglobin immediately; (2) other erythrocytes showed anisopoikilocytosis and spherocytosis with early disruption and disappearance, anemia resulting; (3) all blood cellular elements showed responses to the artificial perfusion state. In this study the abnormal host responses varied greatly.

What factors contribute to these cellular derangements? Quite simply, the placing of blood in

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other than endothelial lined conduits. Pierson and coworkers<sup>22</sup> blamed high degrees of occlusion, excessive revolutions per minute and the resulting high turbulence in roller pumps as a cause of hemolysis. On the basis of these findings, they employed a flat-valved tubing which allows for less regurgitant flow and 60 per cent fewer revolutions in the roller mechanism. In vitro studies show less hemolysis with this technique, but as Galletti<sup>7</sup> pointed out in 1961 (reiterated by others) the significance of hemolysis studies is uncertain in in vitro studies.

Since the flow of blood in a tube and the change of the cross-sectional diameter of a tube is accompanied by pressure drop and shearing forces, and since rotors, pistons and impellers exert various pressure differentials, Blackshear<sup>3</sup> designed several experiments to determine the hemolysis resulting from these phenomena. Whereas excessive pressure (2,000 mm of mercury) produced little hemolysis, sudden expansion was shown to cause an occasional high hemolytic rate. Shear stress limitations were not defined. From these observations, plus occlusion and turbulence, Blackshear concluded that hemolysis appears to be directly proportional to the probability of red cell encounter with the wall of the tube, raised to the second power.

To define a limit to which an organism can be insulted by hemolysis and the chronic need to regenerate red blood cells, Bernstein and Varco<sup>2</sup> conducted several studies. Using normal mongrel dogs they infused hemoglobin and damaged red cells. They also produced chronic anemia by repeated phlebotomy and found the animals capable of withstanding these insults. One would then question such tolerance with an artificial perfusion device in the circulation causing more widespread metabolic alterations. Such changes are alluded to by Bernstein & Varco in describing the doubly increased metabolism of injured red blood cells by way of the hexosemonophosphate shunt. Such sub-lethal damage to red cells, and possibly other cells is due to prolonged perfusion and poses another grim threat to realization of the artificial heart.

As Blackshear has pointed to roughness of the artificial wall and electromedical characteristics of the materials to help understand hemolysis, such considerations are necessary in the prevention of clot formation. Nosé and Kolff<sup>20</sup> reporting recent work, showed clotting to be a continuing problem

in the twin sac silastic heart that they designed. This problem continues to be described in the work and writings of all authors on the subject except in the description of the intraventricular artificial heart by Hall and DeBakey.<sup>9</sup> After Akutsu and Kolff began to use calves for experiments, as they first mentioned in 1963,<sup>1</sup> the clotting difficulties decreased. Some such difficulties were still present, however, in the recent report<sup>20</sup> of six calves surviving for 10 to 31 hours, with minimal clotting found in the pumping chambers at autopsy.

Suture line leaks of air and blood as well as mechanical breakage continue to plague most investigators. In one series the air leakage of the atrial anastomotic lines produced lethal air embolization. In yet another series the connection between caval vessels, the great vessels and the pumping device was performed with the application of rigid metallic rings. The unfortunate consequence of this method of coupling was angulation, with obstruction to blood flow at these sites.

Although clotting is less in calves than in other experimental animals, they show a great propensity for the development of pulmonary edema. This results in a comparatively high loss rate for experiments of this type. As an explanation for the high incidence of pulmonary edema, the investigators cited the anatomical arrangement in the calf and an imbalance between the artificial ventricles resulting from poor homeostatic function on the part of the monitoring device. Hemolysis continues to be a problem in this animal as well.

To maintain proper dynamics various mechanisms have been designed to regulate the rate to physiologic requirement. In 1962, Kolff and his colleagues developed the first electronic device for the control of output. In the same year Barilla developed a fluid amplification system for the same purpose and a year later Burney built and tested a servo mechanism which caused the pump to work in relationship to venous pressure.<sup>14</sup> Refinements of these devices continue through the present review. Work is constantly being done to improve fluid amplification for more exacting control of the artificial system.

Major consideration in all present designs is for further miniaturization of machinery, from portions of the pump down to the last module for control and energy. The apparent ease of decreasing the size of the previously described rotor pump produced the incentive for modification of the tubing used in this device. It is apparent that this



will be true in pumps of other types. In some instances, lack of miniaturization prevented long-term survival of the laboratory animal. Pierce<sup>21</sup> reported that the artificial heart was too big to permit closing the chest of the dog used in an experiment.

In describing their intraventricular artificial heart, Hall and DeBakey said:

"An artificial heart should: be responsive to the body's demands for blood by being capable of altering the cardiac output, i.e. it should maintain adequate perfusion pressure at no expense to venous pressure, be atraumatic to blood and compatible with other body tissues, require no anticoagulant—at least to the point that normal clotting mechanisms would not be significantly altered, be fabricated of strong durable lightweight material—nonrigid, have space and design requirements which would not compromise adjacent organ structures, be easy to insert, have minimal possibilities of immediate or late hemorrhage."

With these salient features in mind this colossal requirement is challenged by a multitude of researchers.

Beyond the scope of total replacement with artificial hearts Gradel and Kantrowitz<sup>8</sup> and Liotta and DeBakey<sup>15</sup> have done encouraging work with the so-called "auxiliary left ventricle." This device when perfected may be placed adjacent to the aorta to support, complement or bypass the output of a diseased and failing left heart.

### The Homograft Heart

The homografted mammalian heart has shown great potential for orthotopic transplantation. Although it is completely denervated it is capable through apparent intrinsic reflex to function well following transplantation, and it handles the circulatory burden without the many aberrations in the bloodstream which are seen with artificial hearts. Survivals are longer and greater in number than with the mechanical substitutes. Immunologic unknowns pose significant drawbacks. Although with cardiac tissue the rejection phenomenon is not manifested in quite the same manner as it is in the more highly specialized cells of the lung, liver and kidneys, rejection is still a stumbling-block. Among other problems for consideration is the method for prolonged storage of organs while host preparation is carried out. Another problem, the procurement of donor tissue, remains to be worked out legally and philosophically.

Alexis Carrel<sup>5</sup> was probably the first to transplant a heart. He placed it in the neck of a recipient animal, where it survived for about 24 hours. In 1960, Lower and Shumway<sup>16</sup> reported their first experiments with orthotopic heart transplants. Successful transplants were performed and the animals survived for as long as three weeks. These investigators reported several technical difficulties at the anastomotic sites of the friable great vessels in dogs, especially in autotransplants where the cuff margin was small. Usually the difficulty was bleeding from the aortic closure site, which was corrected by placing an Ivalon<sup>®</sup>\* bolster about the suture line.<sup>11</sup>

A heart that is to be transplanted immediately is immersed in a bath of saline at 0-4°C, which quickly lowers the temperature of the organ to below 10°C. After 10 to 15 minutes of cooling, the heart is sutured in position—which takes about 60 minutes—without further hypothermia. If this cooling technique was used for more extensive periods, recovery of the heart after the transplant was adversely affected. Seven hours was the longest period of cooling with recovery afterward.<sup>17</sup> In cases in which a heart was kept in the chilling solution for longer than that, either it would not recover at all or, if defibrillation could be performed, the circulatory burden was not assumed.

For more prolonged preservation, techniques are in developmental stages. Bloch and Mannax<sup>4</sup> have used hyperbaric-hypothermia without coronary perfusion. After 24 hours of storage, successful defibrillation was carried out with the heart positioned in the neck of a recipient animal. As these investigators acknowledged, this technique must withstand the test of orthotopic positioning of the heart.

The use of in vitro coronary artery perfusion and hypothermia is still under consideration as a possible method for extending storage time. This has not been universally successful because of early coronary artery branching where direct cannulation is employed and because of aortic valvular incompetency where aortic root perfusion is used. Excessive pressure in this technique may lead to vessel disruption, with interstitial hemorrhage and edema of the myocardium. Another technique that may be applicable is one based on the concept of the intermediate host, using a modification of the Carrel technique. It is possible here

\*Unipoint Industries, Inc., High Point, North Carolina.

to take the donor organ at an appropriate time and protect it in a more normal environment until the time of transplantation.

Closely akin to the discussion of storage is the question of cardiac survival after death of the donor organism. It is becoming increasingly apparent that a delay of 30 to 60 minutes between death of the donor animal and immersion of the heart in cold saline solution is compatible with survival.

Excessive cold used in the short or more prolonged storage is not without incidental abnormality. Lower and Hurley observed atrial arrest with slow nodal rhythm resulting from cold injury to thin atrial tissue. With slight increase in the immersion temperature, this abnormality essentially disappeared. Other conduction abnormalities also result from direct trauma to the nodal or bundle tissue, with resulting idioventricular rhythm.<sup>12</sup> In almost all instances the edema clears and the heart reverts to a supraventricular rhythm, usually sino-atrial. Intermittent Stokes-Adams attacks have been documented as late as six weeks following heart transplantation. In the early postoperative period where the abnormal bradycardic rhythms are present, an external pacemaker is necessary for survival. This may be essential in as many as 50 per cent of all cases, at least for short periods postoperatively.

Once the atrial rhythm is restored it becomes quite stable and is usually sino-atrial or A-V nodal. This stability, plus tachycardia from norepinephrine and absence of tyramine and vagal effects, establishes the denervated state. In autotransplants which were performed for the long-term study of this condition, reinnervation was apparent in 18 to 24 months following operation.<sup>6</sup> Many of the animals are alive and well four to five years after the transplant. With this study it was possible to show that the transplanted heart approaches normal levels of function.

A significant barrier to the clinical use of homologous hearts is the immunologic rejection response. Following orthotopic heart homografting, although normal function will return, this is followed by rejection in an average time of one week. The range may be from several days to three weeks. This response can occur without any change in the temperature of the recipient or in leukocyte count, sedimentation or enzyme studies. Such changes are accompanied by fibrinous pericarditis, edema and hemorrhage of the myocardium. The

degeneration of cardiac muscle and the presence of immunocytes characterize the process.

Hume and coworkers<sup>10</sup> described the serial observation of lactic acid dehydrogenase by which they monitor rejection in renal homotransplants. Even though determination of this enzyme is useful in clinical cardiac studies, in homografts it did not help. In the animals that died with full blown rejection phenomenon the enzyme studies had shown no change. For this reason Lower and Shumway<sup>18</sup> devised an electrocardiographic screening method in which voltage change in the R-wave of lead II was shown to consistently change with rejection. The significant factor here is that this change occurs before the animal fails clinically.

Reemtsma and coworkers,<sup>23</sup> in 1962, used a folic acid antagonist to extend survival times after homologous cardiac transplant in the neck. Utilizing intermittent administration of azathioprine and methylprednisolone, Lower<sup>19</sup> had survivals up to one year following transplants. The intermittency of drug administration was based on electrocardiographic R wave voltage decline as seen in serial lead II electrocardiogram tracings.

Medications have extended viability of donor organs, but recipient function is frequently altered. Lethal or near lethal disturbance to the hematopoietic and reticuloendothelial systems has resulted in most cases of prolonged or excessive use of drugs. The sequelae to therapy may be: empyema, pneumonitis, endocarditis, jaundice, anemia and gastrointestinal hemorrhage.

## Discussion

With superficial discoveries and innovations nearly concluded, the proponents of artificial hearts must now produce significant survivals. The ideal is a perfectly functioning artificial heart which will be in ready supply and in all appropriate sizes for use upon demand.

Procurement of hearts for homografting will not be so easy. Even if medicolegal, emotional, moral and social pressures are ignored, derivation of a firm set of criteria to fit all cases seems nearly impossible.<sup>24</sup> The problem, which will exist in the acquisition of donor hearts for both the young pediatric and the adult group, represents the greatest obstacle to clinical heart homografting.

With or without solution of the immunologic complexities surrounding homografts, advocates of the artificial and grafting philosophies should draw together on common ground. The graft has



proven to be a highly satisfactory substitute but it is prone to rejection and to early insufficiency. It would be indeed valuable to have an artificial heart or heart-lung combination which could function through the early stages following grafting in support of the heart and its recipient. Such support is afforded by dialysis techniques after renal grafting where a graft may not take until a second or third procedure.

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# CASE REPORTS

## Granuloma Inguinale

Report of a Case in California  
With Notes on Pathogenesis

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GRANULOMA INGUINALE is a relatively uncommon venereal disease affecting the skin and subcutaneous tissue and, rarely, other organs. While primarily considered a disease of tropical regions, it has been seen in all parts of the world. In the United States most cases have been reported in the southeast and in the large metropolitan cities of the eastern seaboard. Although less common in California, cases have been reported to the California State Department of Public Health every year since 1939.<sup>2,3</sup> The number of cases gradually increased to a maximum of 80 in 1947. This was attributed to the rise in the Negro population of the state. In the United States granuloma inguinale most often affects Negroes. Fewer than 10 per cent of cases are found in Caucasians. Since 1952 between one and 12 cases have been reported in California annually. It has been during this latter period that antibiotics have been used widely in the treatment of granuloma inguinale and the disease is now infrequently seen even in previously endemic areas such as Georgia. Because of its rarity, many physicians are unfamiliar with the nature of the disease. Moreover, the viral disorder, lymphogranuloma venereum, is often confused with granuloma inguinale.

We recently had opportunity to treat a patient

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with disabling granuloma inguinale and herein report the experience.

### Report of a Case

A 56-year-old Negro man was admitted to the hospital on 27 July 1965 because of a large ulcerated area in the perianal, perineal and crural regions. This was not especially painful.

About four or five years previously he had begun to experience discomfort in the perianal area. He visited a physician in 1963 and was told he had hemorrhoids. Later he noticed an open "sore" spreading slowly from the anus outward and anteriorly. He never felt terribly ill, but did have occasional feverish feelings and chills. He had lost 20 to 30 pounds in the past several years. Defecation had become increasingly difficult and stools were noted to be narrower than usual.

There were no relatives or other contacts with similar illness or tuberculosis. The patient was unmarried and was vague about his sexual life, but when questioned directly denied homosexual experience.

On examination there was an extensive shallow ulceration around the anus, covering a narrow strip in the midline of the perineum, and surrounding the base of the scrotum on the posterior and both lateral aspects (Figure 1). The ulcer continued up into both crural folds, stopping short of the inguinal region. The floor of the ulcer was covered with red, meaty, exuberant, nodular granulation tissue. There was a fairly profuse, foul-smelling seropurulent exudate. The margins of the ulcer were firm, sharp and not undermined. Some narrow areas of regenerating epithelium and scarring were present. The anus was irregularly scarred and there was a tight fibrous stricture high in the canal. There were no pseudobuboes and inguinal adenopathy was limited to a few small shotty nodes bilaterally.

Initial touch smears of exudate stained with Wright's stain showed inflammatory cells and varied cocci and bacilli. Darkfield examination



showed numerous large spirochetes which did not have the morphologic features or the motility characteristic of *Treponema pallidum*. A biopsy specimen showed a non-specific ulceration with chronic inflammation together with bacterial and spirochetal infection at the surface. Staphylococcus and diphtheroids grew on a culture of the exudate. Curettings of granulation tissue crushed between two glass slides and stained with Wright's stain showed many macrophages with cytoplasmic cystic spaces filled with typical Donovan bodies (Figure 2).

The packed cell volume was 31.5 per cent. Leukocytes numbered 6,900 per cu mm with a normal cell differential; the Venereal Disease Research Laboratory test was non-reactive; the purified protein derivative (intermediate) skin test was positive. Serum proteins were 9.6 gm per 100 ml, with a reversed albumin-globulin ratio. The Frei test was just barely positive. The lymphogranuloma venereum complement fixation test was positive in a dilution of 1:80.

The patient was treated with open wet dressings and tetracycline by mouth, 500 mg every six hours for one month. Improvement was noted within a few days and complete epithelization had occurred by the end of the third week. The odor and the exudate disappeared within a week. Daily digital rectal examinations were done and at the conclusion of therapy the patient was able to defecate without discomfort. The ulceration healed

with the formation of a soft partially depigmented scar. The patient's anemia improved on oral iron therapy.

## Discussion

It is not uncommon for patients with this disease to refrain from seeking medical advice until the lesions are large and difficult to hide. This man was able to wait several years. Actual pain in the ulcer was minimal but he had become concerned about the change in his stools. He had a complicating fuso-spirochetal infection which contributed to the exudate and odor but this required no treatment other than the tetracycline administered for the granuloma inguinale.

The etiologic agent of granuloma inguinale is an encapsulated bacillus, *Donovania granulomatis*. It is found residing within large mononuclear cells in the affected tissues and has been cultivated on fresh yolk medium and in chick embryo yolk sac. Although the disease has been reproduced experi-



Figure 1.—View of perineal ulceration extending upward into crural folds and downwards around anus. Patient in lithotomy position with genitalia retracted anteriorly.

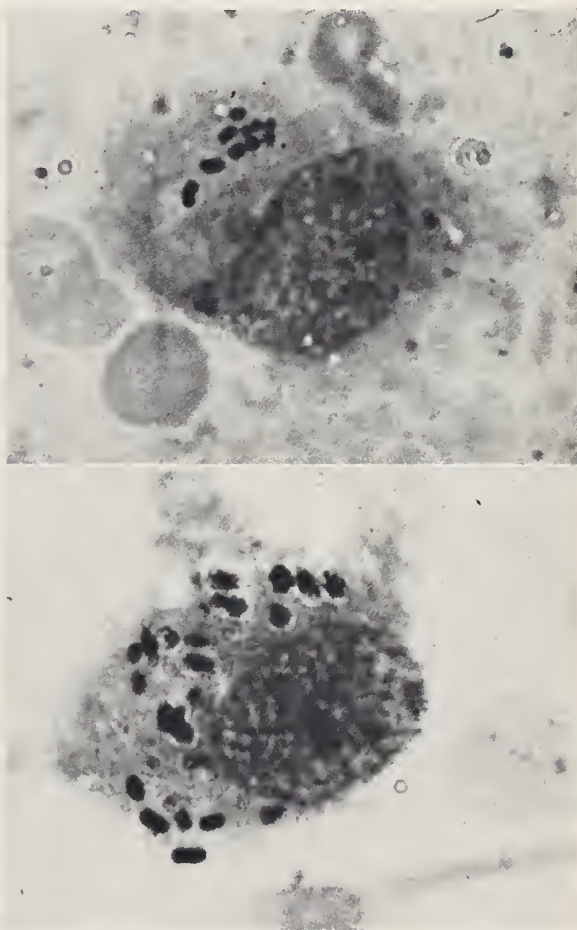


Figure 2.—Large macrophages containing bipolar Donovan bodies ( $\times 950$ , oil immersion).

mentally in volunteers by inoculating pus from pseudobuboes, it has not yet been successfully induced by injection of material grown in culture. Thus, Koch's postulates have not been fulfilled.

Granuloma inguinale is ordinarily classified as a mildly contagious venereal infection. It usually affects the genitals, inguinal and perianal areas and is most often encountered in patients in the third and fourth decades of life.<sup>7</sup> However, reported instances of conjugal infection are rare<sup>1</sup> and the venereal nature of the disease is not finally settled. Recently immunologic and cultural similarities between *Donovania* and certain enteric bacilli were demonstrated.<sup>5</sup> It is quite likely that the organism has a fecal habitat and that inoculation into the skin may occur when appropriate trauma is coupled with fecal contamination. It is possible that organisms from a patient's own enteric tract are inoculated and thus the disease would be venereal only in relation to trauma from a sexual partner. Reported cases of perianal granuloma inguinale in male homosexuals who practice rectal coitus are not infrequent,<sup>4</sup> a fact that bears particular emphasis in light of the importance of the homosexual population in the current upsurge in venereal diseases.<sup>8</sup> A diagnosis of "hemorrhoids" may be made at first, as in the present case, and definitive therapy unnecessarily postponed.

The incubation period is unknown, but in experimental infections it is about 50 days.<sup>9</sup> The initial lesion in the male is usually on the glans, the prepuce or the shaft of the penis. In the female, it is frequently on the labia or the vaginal orifice. These early lesions are vesicular, papular or nodular and may be evanescent. They often ulcerate and become covered by an exuberant "beefy-red" granulation tissue which is raised above the surface of the surrounding skin. The lesions spread by peripheral extension, by autoinoculation, via the lymphatics and, rarely, by hematogenous dissemination. Inguinal ulceration is common and may be preceded by the formation of a fluctuant swelling in the groin called a pseudobubo. The latter is not a swollen lymph node, but rather a granulomatous inflammation of dermis and subcutaneous tissue which subsequently erodes the surface. In addition to the exuberant and ulcerative types, cicatricial lesions may be seen as more or less healing takes place.

Untreated, the disease progresses slowly but relentlessly. The foul-smelling lesions enlarge, often becoming secondarily infected with fuso-spiro-

chetal organisms. The patient may be febrile and anemic. Loss of weight is common. Extreme cachexia and death may ensue.

The clinical appearance of the lesions and the demonstration of the Donovan bodies enable one to make a diagnosis. Casual smears or swabs of the surface of the lesion are inadequate for demonstrating the organisms. A piece of granulation tissue from the border should be obtained with or without previous infiltration anesthesia. It may be snipped off with scissors or curet or obtained with a punch biopsy forceps. It is then crushed between two glass slides. After drying in air, these slides are stained with either Wright's, Giemsa's or pinacyanole stain and examined under oil immersion. The Donovan bodies are 1 to 1.5 microns long<sup>6</sup> and lie in cystic spaces within the cytoplasm of large mononuclear cells. They are encapsulated, the capsule staining pink with Wright's stain. Their bipolar appearance has been likened to that of a closed safety pin. Although some bodies may be found extra-cellularly, particularly if the tissue has been crushed too vigorously, intracellular parasites should be sought, inasmuch as other contaminating bacilli may be present in the exudate.

Histopathologic examination of a biopsy specimen may be necessary although in many cases the organisms are more easily seen by the crush-smear technique described. An acute and chronic granulomatous inflammation without tubercle formation is seen histologically. In addition, marked pseudoepitheliomatous hyperplasia is commonly present at the edge of the ulcer. In sections, Donovan bodies are best seen with a silver stain such as Dieterle's.

The Frei skin test for lymphogranuloma venereum is negative—unless, of course, the patient has had that disease. That this event may be more common than is ordinarily supposed is indicated by Goldberg,<sup>5</sup> 50 per cent of whose patients with granuloma inguinale also had diagnostically positive complement fixation serologic tests for lymphogranuloma venereum. Indeed, there is a tendency for multiple venereal diseases to occur in populations having a high rate of one or another of the infections.

Two grams of a broad-spectrum antibiotic (tetracycline, oxytetracycline, or chlortetracycline) are given orally each day for two to four weeks. Alternatively, streptomycin may be given intramuscularly, 4 gm in divided doses daily for five days, a total of 20 gm. These programs are ordi-



narily effective. Donovan bodies disappear from the lesions within a few days and rapid healing of lesions takes place over the following week or two. Relapses may occur up to several years after healing<sup>9</sup> but these usually respond to retreatment. Serologic tests for syphilis should be done monthly for four months after treatment, since syphilis may have been acquired simultaneously with granuloma inguinale.<sup>10</sup> Deformities such as anal stenosis caused by scars may have to be corrected surgically after antibiotic therapy has been completed. Post-treatment biopsy should be done of any portion of the lesions that do not heal inasmuch as chronic granuloma inguinale has at times been complicated by the development of carcinoma in the area involved.<sup>11</sup>

## Summary

A patient with perianal ulceration caused by granuloma inguinale was not promptly treated for that condition, as the symptoms had been attributed to hemorrhoids.

Granuloma inguinale is a bacterial infection readily susceptible to treatment with antibiotics. While not common, its presence should be suspected in all cases of ulceration involving the genitalia, inguinal region and perianal area.

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# Infectious Mononucleosis With Central Nervous System Involvement

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IN 1931, Epstein and Damshek,<sup>6</sup> and Johansen<sup>11</sup> independently described the first cases of central nervous system involvement in infectious mononucleosis. Since that time there have been at least 78<sup>7</sup> well-documented cases reported in the English literature with 20 (Table 1) occurring in the pediatric age group—16 years or younger.

"The present concept of infectious mononucleosis," according to Silver and coworkers<sup>20</sup> "is that it is a generalized systemic disease of unknown origin with cellular infiltration in almost every organ of the body, the clinical picture varying with the predominant site of involvement. When the central nervous system is involved, the manifestations also vary, depending upon the site implicated."

The central nervous system involvement may precede, follow or occur simultaneously with the usual manifestations of the disease.<sup>2,14,20</sup> However, of the 20 pediatric cases reported, there were only three<sup>5,16,20</sup> in which the central nervous system symptoms occurred first. In two<sup>5,16</sup> of these, the nervous system involvement was the only manifestation.

We are, therefore, reporting a further case of infectious mononucleosis in which involvement of the central nervous system produced the presenting symptoms.

## Report of a Case

A girl 11½ years old was admitted to Childrens Hospital on 17 September 1964 with a history of

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fever and extreme lethargy for four days and hallucinations and vomiting on the day of admission. On physical at the time of admission, lethargy, decreased ability to concentrate, slurred speech and slightly ataxic gait were noted.

Leukocytes numbered 5,400 per cu mm, with 65 per cent lymphocytes. The cerebrospinal fluid pressure was normal. The fluid contained no cells; protein and sugar content were 52 mg and 57 mg per 100 ml, respectively. An electroencephalogram showed generalized delta activity, especially in the left hemisphere. Heterophile antibody titer the day after admission was 1:224, and 1:56 after guinea pig kidney absorption.

Two days after admission, the liver was tender and the edge was palpated 1 cm below the right costal margin. The urine was dark. Laboratory studies at this time showed serum bilirubin 1.8 mg per 100 ml direct and 1.0 mg per cent indirect, urine urobilinogen positive in 1:64 dilution, SGPT 610 units, and SGOT 217 units. By the fourth hospital day, hallucinations and lethargy had gradually disappeared and the patient was alert but still weak. The cerebrospinal fluid at this time was under normal pressure. It contained one lymphocyte per field, 28 mg of protein and 57 mg of sugar per 100 ml.

Laboratory studies eight days after admission

TABLE 1.—Data on 20 Cases of Pediatric Infectious Mononucleosis with Central Nervous System Involvement

Author	Age	Sex	Diagnosis	Heterophile	CSF		Comments
					Protein mg per 100 ml	Cells Per field	
Davidson <sup>4</sup>	16		Encephalitis	1:896	—	18	Outcome not mentioned.
Geliebter <sup>9</sup>	10		Encephalomyelitis	1:256	400	9L	Complete recovery in 51 days.
Bonyng <sup>3</sup>	14		Optic neuritis	1:1792	55	6	Treated with BAL with encouraging results. Normal vision with some residual optic atrophy.
Karpinski <sup>12</sup>	9	M	Meningoencephalitis	1:128	76	33L, 2P	Complete recovery.
	3	M	Meningoencephalitis	1:128	45	100L 95P	Complete recovery. EEG showed slow delta foci in occipital region.
	9	M	Encephalomyelitis	1:1024	30	36L	Paralysis of lower extremities and urinary incontinence.
Raftery <sup>17</sup>	16	M	Gullian-Barré	1:1792	280	—	Residual weakness in lower extremities. Positive CSF heterophile.
Walsh <sup>22</sup>	8	M	Encephalitis	1:1024	256	7	Slight intention tremor at 6 weeks after onset. EEG showed generalized slow wave abnormality which improved; but persisted for 2 months.
Durfey <sup>5</sup>	*4	F	Gullian-Barré	1:1792	—	70	Complete recovery at 3 months. CSF heterophile was positive.
Silver <sup>20</sup>	*9	M	Encephalomyelitis	1:640	51	25L 5P	Complete recovery. EEG showed diffuse and non-specific changes.
Montandon <sup>13</sup>	6½	M	Gullian-Barré	1:300	Increased	176	Outcome not mentioned.
Shechter <sup>18</sup>	6		Retrobulbar neuritis	1:224	—	—	Complete recovery.
Pew <sup>16</sup>	21 mo.	F	Encephalitis	1:112	—	—	Complete recovery with subsequent febrile seizures.
	15	F	Encephalitis	1:498	Normal	Normal	Complete recovery.
	* 11	M	Encephalitis	1:896	128	8P 5L	Coma for 10 weeks with resultant severe brain damage. EEG showed diffuse depression consistent with encephalitis.
	7	M	Gullian-Barré	1:5120	60	0	Died secondary to pulmonary complications. Autopsy revealed essentially negative CNS.
Sharfatz <sup>19</sup>	14	F	Meningoencephalitis	1:1792	—	74L 6P	Complete recovery in 28 days.
Nichols <sup>15</sup>	7	F	Encephalitis	1:112	50	30	Complete recovery.
	8	F	Encephalitis	1:1792	44	51	Complete recovery.
Evans <sup>8</sup>	6		Bilateral External Ophthalmoplegia	1:448	35	4	Complete recovery in 24 days.

Code: L—lymphocytes; P—polymorphonuclear cells; EEG—electroencephalogram; CSF—cerebral spinal fluid.

\*Presented with central nervous system involvement.



showed the heterophile antibody titer to be 1:448, SGPT 485 units and SGOT 365 units. Leukocytes numbered 12,100 with 85 per cent lymphocytes, many of which resembled Downey cells types I and II. Except for tenderness over the right costal margin and slight weakness, the patient was clinically asymptomatic and was discharged from the hospital with instruction for continued observation.

Sixteen days after the onset of illness, the patient's liver was not enlarged or tender, but the spleen was enlarged to 3 to 4 cm below the left costal margin on inspiration. The heterophile antibody titer was 1:448, and was 1:224 after guinea pig kidney adsorption. SGPT was 1,060 units and SGOT 640 units.

One month after the onset of illness, the patient felt well but the spleen was enlarged to 2 cm below the left costal margin and the liver was minimally tender to percussion although not enlarged.

At the end of another three weeks the splenic enlargement and hepatic tenderness were no longer present. The heterophile antibody titer was 1:112, SGOT 55 units and SGPT 100 units.

Viral cultures taken at the time of admission from throat, stool and two cerebrospinal fluid specimens were negative. Cultures from throat, stool and blood taken seven weeks after onset of illness were also negative. An electroencephalogram seven weeks after the onset of illness showed some apparent residual of minor changes in the left occipital area.

## Comment

The incidence of neurologic complications in infectious mononucleosis is probably less than 1 per cent<sup>7,15,19</sup> if cerebral spinal fluid pleocytosis alone, without clinical symptoms, is excluded.<sup>21</sup>

Various neurologic complications occur, with serous meningitis (meningeal symptoms without abnormal cerebral spinal fluid findings), meningitis (meningeal symptoms with abnormal cerebral spinal fluid findings), encephalitis, encephalomyelitis (brain and spinal cord involvement), acute polyneuritis (Gullian-Barré), peripheral neuritis and optic nerve involvement having been reported.<sup>1,2,7,10,20</sup>

With the exception of serous meningitis and peripheral neuritis, each of the above complications has been reported in the pediatric age group (Table 1).

Cerebral spinal fluid findings have been variable, with elevations in protein and cell count oc-

curing independently or together (Table 1). As to the outcome in the 20 cases reviewed here: 13 patients had complete recovery, four patients had residual neurologic deficits (one with severe brain damage), one patient died and in two instances the final outcome was not mentioned but was presumed to be favorable. Therefore, there was a 20 per cent morbidity and a 5 per cent mortality rate in the cases reported.

As noted above, there have been only three<sup>5,16,20</sup> previous case reports of central nervous system involvement as the initial manifestation of infectious mononucleosis. Silver<sup>20</sup> reported the case of a nine-year-old boy in which a grand mal seizure was the first symptom noted. In that case the initial physical examination and blood studies did not implicate infectious mononucleosis. However, on the morning following admission the patient had exudative tonsillitis with splenic fullness. On a smear of peripheral blood, 29 per cent of the lymphocytes were atypical.

Pew<sup>16</sup> reported the case of an 11-year-old boy who had a grand mal seizure after three days of febrile illness. Subsequently clinical symptoms compatible with encephalitis developed and there was residual brain damage. The only implication of infectious mononucleosis was a positive heterophile of 1:896 after guinea pig adsorption. Likewise, Durfee<sup>5</sup> reported on a six-year-old girl who came to medical attention with a Gullian-Barré syndrome and had no further manifestations of infectious mononucleosis. A positive heterophile of 1:1792 was the only diagnostic clue available.

In the present case, the clinical symptoms at the time of first examination were those of encephalitis. Later hepatosplenomegaly and laboratory evidence of hepatic dysfunction developed. However, clinically only hepatic tenderness and enlargement suggested the diagnosis of infectious mononucleosis, a diagnosis that might not have been confirmed had not blood smears been examined and the heterophile antibody determination carried out.

The authors believe that infectious mononucleosis should be considered and a heterophile antibody determination performed in any case in which there are unexplained acute central nervous system disorders at the outset.

## Summary

A case of infectious mononucleosis presenting with neurologic involvement is reported. In three of the 20 previously reported pediatric cases of

infectious mononucleosis with neurologic complications, central nervous system manifestations were the first symptoms. In two of the three, heterophile determination gave the only clue implicating infectious mononucleosis. Infectious mononucleosis should be considered in the differential diagnosis of any case in which unexplained acute bizarre neurologic complaints are among the first symptoms.

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## Myasthenia Gravis with Thymic Tumor

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SURGICAL REMOVAL of the normal thymus in the treatment of myasthenia gravis is a well recognized procedure. When a true thymic tumor is present, removal of the gland for the treatment of myasthenia is conjectural.

The usual indication for thymic removal in myasthenia gravis is the locally invasive tendency of the tumor and the hope of alleviation of the symptoms in a patient with myasthenia that is refractory to treatment.

The present report concerns an adolescent boy who when first seen had x-ray evidence of a large mediastinal mass, and then rapid onset of myasthenia gravis. The case had interesting facets: the youth of the patient, the rapid onset of symptoms and a return to control through drug therapy after removal of the tumor.

### Report of a Case

A 17-year-old Mexican boy was admitted to the hospital on 16 July 1964 with the chief complaints of extreme fatigability, muscular weakness, weight loss of 20 pounds and shortness of breath of two months' duration. He had been entirely well until the onset of the symptoms. There was no history of fever, night sweats, diarrhea, nervousness or intolerance to heat.

On physical examination the patient, who was lying in bed, was asthenic and apathetic. Generalized muscle wasting was apparent. The temperature was 36.9°C (98.4°F), the pulse rate 84 and regular, blood pressure 110 mm of mercury systolic and 70 mm diastolic. No evidence of lymphadenopathy was present and no abnormali-

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ties were noted visually or on palpation and auscultation of the neck, chest and abdomen.

The pertinent physical findings were limited entirely to the neuromuscular system. Both eyelids drooped. Total muscular ophthalmoplegia was noted, with eye movement being decidedly limited in all planes of motion. The eye movements became progressively weaker with activity and the patient was totally unable to lift his eyelids above the horizontal plane. The pupils reacted to light and no nystagmus was noted. There was generalized muscle weakness which became progressively worse on exercise, but no evidence of fasciculation or localized muscle wasting. The deep tendon reflexes were equal and no abnormal reflexes were elicited. Sensibility was not disturbed and the patient's appreciation of touch, pinprick, heat, cold, posture, passive movement and vibration was intact. An intravenous injection of 10 mg of edrophonium (Tensilon®) was given, slowly, and a dramatic improvement of muscle strength followed. Most pronounced were the return of full range of eye motion and the complete regression of ptosis.

**Laboratory Data:** The urine gave a negative reaction for albumin, glucose and bile. The sediment showed no casts and only one white blood cell per high-power field. The hematocrit was 51 per cent. Leukocytes numbered 8,000 per cu mm, with 65 per cent neutrophils, 2 per cent band forms, 4 per cent eosinophils, 28 per cent lymphocytes and 1 per cent monocytes. Serum electrolytes were: sodium 143, chlorides 105, potassium 4.4, and bicarbonate 32 mEq per liter. Results of blood chemical studies: serum calcium 10.6 mg and serum phosphorus 3.9 mg per 100 ml, protein-bound iodine was 4.8 micrograms per 100 ml, and tri-iodothyronine resin uptake 30.5 per cent. Serologic tests for syphilis were negative.

The spinal fluid was clear and colorless, and under normal pressure. Spinal fluid sugar and protein were within normal limits, as was a simultaneous determination of blood sugar. No leukocytes were seen in the fluid.

An electrocardiogram showed a normal sinus rhythm with right axis deviation.

X-ray films taken on admission (Figure 1) showed an increased density overlying the right heart border, interpreted as being consistent with thymoma.

An intravenous angiogram with 50 ml of 75 per cent Hypopaque® showed compression of the

right heart border by a smooth extrinsic mass (Figure 2). The heart was otherwise normal in size.

Administration of pyridostigmine bromide (Mestinon®) 60 mg every four hours, was begun, with only slight and transient improvement. Despite an increase in dosage to levels approaching 1 gm daily, the patient's symptoms of fatigability and weakness were not controlled and further measures were indicated.

On 29 July, thoracotomy was performed and a thymic tumor measuring  $9.5 \times 9.5 \times 3.5$  cm, was removed (Figure 3). The tumor was lobulated and attached to the upper anterior mediastinum by a stalk measuring  $4 \times 3 \times 2$  cm. Microscopic sections of the tumor showed large sheets of tightly-packed



Figure 1.—X-ray film of chest showing increased density overlying the right heart border.

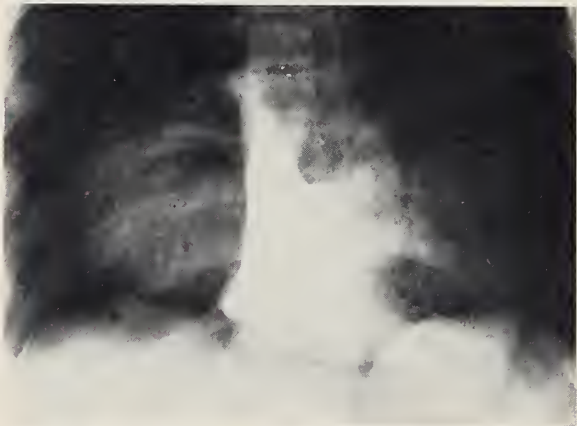


Figure 2.—Compression of the right heart border is shown in this intravenous angiogram.

small cells with normal nuclei and scanty cytoplasm and poorly defined cell borders. These cells were separated by broad septa of dense fibrous connective tissue. Large portions of the tumor showed homogeneous simple necrosis and, in some of the necrotic areas, cholesterol crystal slits surrounded by multi-nucleated giant cells were seen. This appearance is characteristic of a benign thymoma of the lymphocytic type.

Upon completion of thoracotomy, tracheostomy was performed for better tracheal toilet, and respiration was maintained with the aid of a Morsch fixed cycle respirator for several days and, subsequently, with a Bird respirator.

The postoperative course was complicated by a superficial incisional abscess for which appropriate measures were undertaken with good results.

The patient was discharged on 4 September 1964, well controlled on 720 mg of pyridostigmine daily.

Kept under close observation for more than a year now since the operation, the patient was readmitted to hospital three times in the first six months, for left lower lobe pneumonia on two occasions and bronchitis on the third. In the nine months preceding this report, the patient had re-

mained well controlled on oral administration of pyridostigmine, 120 mg at 8 a.m., noon and 4 p.m., plus long-acting pyridostigmine, 360 mg at 8 p.m.

In the present case use of pyridostigmine bromide following operation to remove a thymic tumor kept symptoms well controlled. In most cases of myasthenia gravis the failure in neuromuscular transfer is due to a lack of "acetylcholine effect," resulting in insufficient depolarization of the motor endplate. Several drugs, called anticholinesterases, can be used to decrease the destruction of acetylcholine, among them edrophonium chloride, neostigmine bromide and pyridostigmine bromide. For regular maintenance, pyridostigmine bromide is preferable because of ease of administration and extended action.

## Discussion

Thymectomy is usually performed in patients with myasthenia gravis under 40 years of age. The incidence of clinically detectable thymoma in myasthenia gravis has been variously reported as 12 to 15 per cent and has been most generally noted in the third to fifth decades.<sup>1,2,6,7</sup> Simpson,<sup>6</sup> in a series of 294 patients who had thymectomy, found 36 cases of thymoma, 13 occurring in males. The mean average age of those with thymoma was 39.3 years, and none was less than 24 years of age. Keynes<sup>4</sup> also remarked on the low incidence (4 per cent) of thymoma and myasthenia gravis in persons under 30 years of age.

Viets and Schwab<sup>7</sup> noted that the prognosis of myasthenia gravis with thymoma is especially poor in males irrespective of the therapy. Local invasion of thymic tissue is a danger because of the location of the tumor in the mediastinum in approximation with the great vessels and the heart. Ellis<sup>2</sup> said that about 25 per cent of thymomas are locally invasive or locally implant on pleural surfaces, while Kreel suggested that the malignant potential (based on gross appearance and fixation to surrounding tissue) of thymoma is far higher—up to 80 per cent.

In most clinics, decisions for thymectomy are made with extreme selectivity. However, it is generally accepted that a thymoma should be removed because of the local invasiveness of the tumor.<sup>3,7</sup>

In a review of the literature few reports were found of thymomectomy in myasthenic patients under 20 years of age, and in all cases the patient was a female.



Figure 3.—Photograph of thymoma cut to reveal large lobulations and areas of necrotic tissue.



## Summary

A case of myasthenia gravis associated with a large thymoma has been presented. The patient was a 17-year-old boy. Thymomectomy was carried out and the patient did well thereafter while receiving pyridostigmine by mouth.

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### Generic and Trade Names of Drugs.

Edrophonium—*Tensilon*.

Pyridostigmine—*Mestinon*.

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# Leiomyoma of the Duodenum As an Unsuspected Source of Bleeding

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*Martinez*

A 21-YEAR-OLD white male laborer was admitted to the hospital on 10 July 1957 because of tarry stools of one day's duration, accompanied by dizziness, weakness and increased thirst. There had been no pain. He had been in hospital twice before within the year preceding, from 17 August to 31 August 1956, and from 2 April to 16 April 1957, both times for duodenal ulcer with hemorrhage. During the first period in hospital he had received

nine units of whole blood. He said that he had a medical discharge from the Navy because of duodenal ulcer.

The patient was thin, weighing 132 pounds. The pulse rate was 95 and blood pressure 110/70 mm of mercury. The conjunctivae were pale. There were scattered *cafe au lait* spots over the whole body. No abnormalities were noted on percussion and auscultation of the heart and lungs and palpation of the abdomen.

Hemoglobin content of the blood was 10.1 gm per 100 ml, the hematocrit 35 per cent and leukocytes 8,250 per cu mm with a normal differential of cells. A serologic test for syphilis was negative and results of urinalysis were within normal limits.

After several days of medical management with restricted diet, antispasmodics and antacids, the bleeding subsided. On 12 July, x-ray examination of the upper gastrointestinal tract showed "marked obstruction to the gastric outlet and a rounded indentation on the superior side of the juncture of the second and third portions of the duodenum" (Figure 1). A second area of indentation was also noted in the third portion of the duodenum distal to the first. No abnormalities were noted on barium enema study.

On gastroscopic examination a slight convexity of the greater curvature portion of the antrum was noted, suggesting external pressure.



Figure 1.—Note two rounded indentations on the superior aspect of the second and third portions of the duodenum.

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X-ray studies of the upper gastrointestinal tract were done again on 24 July, and this time were reported as showing a persistent duodenal ulcer with some evidence of retention. No mention was made of the previously noted irregularities in the lower duodenum.

The patient was transferred to the Surgical Service on 29 July with the diagnosis: (1) Duodenal ulcer; (2) Suspicion of external mass in region of duodenum, possibly a neurofibrosarcoma.

At operation 5 August 1957, a few adhesions were noted in the region of the second portion of the duodenum, but there was no demonstrable ulcer. On inspection of the remaining duodenum a firm nodule 3 or 4 cm in diameter was found proximal to the ligament of Treitz and protruding toward the pancreas. On biopsy of a frozen section the nodule was reported as leiomyoma. The duodenum was then mobilized both to the left and right, the third and fourth portions being freed up from beneath the superior mesenteric vessels. A second smaller nodule was discovered to the left of the larger mass. The segment of the duodenum containing the two tumors was resected and the duodenal continuity was restored by a two-layered end-to-end anastomosis. On exploration of the peritoneal cavity no further evidence of disease was found. The patient withstood the procedure well and was given 500 ml of whole blood during operation.

### Pathologist's Report

The specimen was described as consisting of a 7 cm segment of intestine incorporating a mass measuring 3 cm in diameter and having three ulcerations on its surface. A smaller similar lesion 1 cm in diameter lay adjacent to it (Figure 2). On section, the surface bulged and presented a whorl. It was grayish-tan with numerous finer trabeculated areas of a grayish to purplish appearance. There were several large purplish areas of hemorrhage.

Microscopic examination was consistent with leiomyoma save for one area in which larger pleomorphic cells with large bizarre hyperchromatic nuclei with mitosis in several places. No blood vessel invasion was demonstrated. Sections of the smaller tumor were similar but practically no pleomorphism was noted. The microscopic diagnosis was leiomyoma of the duodenum showing focal sarcomatous change.

The patient recovered and was discharged on the 36th hospital day.

In the next two years there was no recurrence of symptoms, but on 7 July 1959, the patient was readmitted a day after passing tarry stools. No source of bleeding was discovered on complete clinical examination and on 6 August the abdomen was opened again. A leiomyoma of the mid-jejunum, subserosal in location was found, along with an area of ectasia at the distal ileum. The leiomyoma was removed by a wedge resection and the ectatic area of ileum was segmentally resected. On inspection of the previous operative site no evidence of recurrence was noted, and the remainder of the viscera were normal to inspection and palpation.

On microscopic examination, the tumor was described as a benign subserosal leiomyoma of the jejunum. The ectatic segment of ileum showed well preserved muscle with alternating areas of lymphoid collections with true germinal centers. Capillary stasis was noted in the densest areas of lymphoid hyperplasia and it was felt that this friable tissue had been the source of bleeding. The



Figure 2.—The specimen removed at time of operations shows the larger lesion uppermost with ulcerated areas. The smaller tumor is visible at the lower portion of the picture.



patient was discharged, well, on the 48th hospital day and at the time of last report had not returned for any further treatment.

## Discussion

Ewing<sup>4</sup> said that leiomyomas of the duodenum are not uncommon and cited Nazzari as having reported some 140 cases. Even so, reports of the lesion appear uncommonly in the surgical literature. Most reports deal with postmortem observations. For example, Willis<sup>7</sup> reported the case of a 46-year-old woman with a history of several attacks of melena over a period of seven months. At necropsy a leiomyoma of the second portion of the duodenum was found. It arose from the lateral wall and was 4 cm in diameter; lobulated and had ulceration of the underlying mucosa.

According to Ewing, Boetticher and Lodi, three types of intestinal myoma exist:

1. Small multiple nodular or polypoid tumors that arise from local proliferation in the muscularis. In this type the mucosa is free.

2. Broad thick tumor masses that form in the muscle layers, the mucosa becoming adherent to the tumor.

3. Large polypoid subserous myomas which may project into the peritoneum.

Starr and Dockerty<sup>6</sup> of the Mayo Clinic noted that the first intestinal myomata were reported by Förster and by Rokitansky and were benign asymptomatic growths. They also cited a case reported by Pellizzari in 1875 of a young girl with an ileocecal myoma who passed the tumor, weighing 1 pound, per rectum. Of the series of 76 tumors reported by Starr and Dockerty, 35 were benign and 41 were malignant.

Ackerman<sup>1</sup> said that smooth muscle tumors may occur in any segment of small intestine and may grow in any of the muscle layers including the muscular mucosa either within or outside the lumen. There is often a central niche similar to that seen in similar tumors in the stomach. If cellular and soft they may be suspected of being malignant. Seldom are there regional metastatic lesions, for these tumors tend to invade the blood stream and metastasize distantly. The microscopic differentiation between benign and malignant may be difficult. Those with many mitotic figures are malignant. However, on occasions some well-differentiated tumors sparse in mitotic figures will later be found to have metastasized.

An excellent review of benign neoplasms of the

small intestine was made by River and coworkers.<sup>5</sup> They said that the possibility of such a tumor should be considered in cases of intestinal tract bleeding when investigations of the stomach, duodenum, gall bladder and colon fail to reveal the cause. Of 81 fibromyomas in one group of cases, 12 were located in the duodenum, 17 in the jejunum, 35 in the ileum, and two at the jejunoileal junction. In 15 cases the exact site was not stated.

Acute intestinal obstruction, Rivers and coworkers said, is the first complication that brings these tumors to clinical notice. Hemorrhage is the second most common sign. In the series they studied, the evidence of bleeding was variously occult blood in the stool, tarry stools, melena and blood on the examining finger. They noted that anemia of varying severity, in the absence of other dominant symptoms, often led to incorrect assumptions and inappropriate treatment. This often resulted in multiple admissions to hospital for diagnostic study, with repeated x-ray examinations that did not help. Ebert and Zuidema<sup>3</sup> said that of all primary small intestinal tumors the ulcerated submucosal leiomyoma was the lesion most often associated with massive hemorrhage.

The ileum is the most common site and they are about equally divided between the jejunum and the duodenum. The complications of obstruction and bleeding are the most usual. Peritonitis through perforation is mentioned in the literature. Malignant change constitutes another complication. Cherry and Hill<sup>2</sup> said that one in six of subserosal leiomyomas undergoes sarcomatous degeneration. In this regard it should be emphasized that the pathologist may have considerable difficulty in distinguishing between benign and malignant smooth muscle tumors of the small intestine.

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# Medical Staff Conference

## Acute Renal Failure

*These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.*

DR. LAWRENCE Z. STERN:\* The patient is a 53-year-old white man, a steelworker, who was admitted to the hospital for evaluation and treatment of acute renal failure. He had smoked two packs of cigarettes a day for over 30 years but was well until, nine months before admission, he noticed a slight tickling sensation in his throat. Eight months before admission his dentist noticed a mass growing in the posterior pharynx. Soon afterward, on diagnosis of carcinoma of the larynx, total laryngectomy and right radical neck dissection was performed. The patient did well and after several months returned to work. On the day before the present admission to hospital, he had a generalized convulsive seizure followed by several more seizures that evening. He had had no past history of a convulsive disorder, and there had been no exposure to toxic chemicals or drugs. The day following the seizures he was admitted, in status epilepticus, to a hospital in his community. At that time the body temperature was 41.5°C (106.8°F) the seizures were controlled with intravenous diphenylhydantoin (Dilantin®) and phenobarbital. There had been no fall noted in blood pressure throughout the course of illness. Urine output was 1,100 ml on the first day. It dropped, however, to 300 ml on the second day and was down to 100 ml per day by the fifth hospital day. Serum creatinine, which had been normal on admission, rose to 11.0 mg per 100 ml. On the seventh day, urine output rose slightly to

128 ml. In an attempt to effect diuresis, he was given 25 gm of mannitol intravenously, and at the same time a continuous intravenous infusion of mannitol was started. Over the next four days the patient received 1,500 ml of 20 per cent mannitol per day. During this period, urine output rose to a peak of 750 to 800 ml a day. However, on the tenth hospital day the output again dropped sharply. At that time the patient was noted to have acute parotitis, which was treated with intravenous penicillin and chloramphenicol. Elevated serum potassium levels were corrected by administration of potassium resin. Peritoneal dialysis was attempted but was mechanically unsuccessful. The patient was then transferred to this hospital.

On admission he was stuporous, was twitching constantly, and his breath had a uremic odor. The pulse was 100 and regular, respirations 28 to 30 per minute, blood pressure 156/90 mm of mercury and temperature 36.5°C (97.7°F).

On physical examination, signs of bilateral pleural effusion and pneumonia were noted, a pericardial friction rub was heard and the abdomen was tender but difficult to evaluate because there was fluid within the subcutaneous tissues.

Packed cell volume was 37 per cent and leukocytes numbered 18,600 per cu mm with a shift to the left. Serum sodium was 118 mEq, potassium 2.8 mEq, carbon dioxide 14.8 mEq, and chloride 72.5 mEq per liter. Serum creatinine was 13.6 mg per 100 ml, blood urea nitrogen 116 mg per 100 ml, and serum osmolality 417 milliosmoles per kg of water.

\*Intern in the Department of Medicine.



On the evening of admission hemodialysis was carried out for six hours, during which the serum osmolarity fell to 246 milliosmoles, creatinine to 7.8 mg and serum electrolytes returned to normal, the patient becoming quite alert. In the next few hours diuresis began and the total urinary volume reached six liters per day. From then on, there was rather dramatic and remarkable recovery from renal failure.

Recovery was complicated by pneumonia (*Pseudomonas aeruginosa* was cultured from sputum) which has been successfully treated with low doses of colistin. A density has appeared on an x-ray film of the chest which may represent a recurrence of laryngeal carcinoma or a second primary neoplasm.

DR. WARREN RUSSELL:\*\* A film of the chest taken on the day of admission demonstrated a diffuse\* increased density in both lung fields, but particularly on the right. Part of the density was due to an effusion. Following therapy, the lungs

were shown to be clear except for a large lesion which appeared at the right base. As it was a solitary large mass, it was considered most likely a second primary neoplasm, but a metastatic or even a granulomatous lesion could not be excluded. An intravenous pyelogram demonstrated rather poor concentration bilaterally but no evidence of obstruction.

DR. PAUL F. GULYASSY:† The unusual derangements encountered in this patient make an excellent introduction to a discussion of the therapy of acute renal failure. We can come to generalities later, but first the case at hand:

This patient had moderate azotemia and hyponatremia, and clinical examination showed a decided increase in extracellular fluid volume as evidenced by extreme pitting edema. In addition, one could infer other extremely important disturbances. The serum osmolarity when first measured was 417 milliosmoles per kg of water. If one takes

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Figure 1.—X-ray film of chest on admission showing diffuse increased density in both lung fields but greater on the right.

the sum of the serum sodium concentration and the blood glucose and adds an additional factor of approximately 10 to 15, as was shown by the very extensive studies of Dr. Isidore Edelman and Dr. Frank Gotch, a very close approximation of the actual serum osmolarity may be obtained unless there is present some other osmotically active substance. In this patient the sum of all the osmotically active substances was approximately 300 milliosmoles, leaving an osmotic gap of 117 milliosmoles per kg of water, which we infer is the concentration of mannitol. This means that the concentration of mannitol was approximately 2,100 mg per 100 ml in the extracellular space. The administration and retention of so large a quantity of a substance which is retained in the extracellular fluid volume produces a series of consequences, some of which are obvious, some not. As one injects hypertonic solutions intravenously, there is movement of water out of the cells into the extracellular fluid space along the osmotic gradient, and dilution of the serum sodium concentration results. In this patient serum sodium was 118 mEq per liter when he entered the hospital. This change may also be due to urinary

sodium losses. The movement of water out of cells causes cellular dehydration, which is very difficult to estimate. However, in this patient, the extent to which the blood mannitol was raised above and beyond the depression of serum sodium concentration suggests a 25 per cent loss in intracellular water at the time treatment was begun.

We were faced with three problems: an extraordinary degree of hyperosmolarity, pronounced expansion of the extracellular fluid volume, and decided contraction of the intracellular fluid volume. Therapeutically, two changes had to be made: one was to expand and dilute the intracellular volume to normal, and the other was to contract and dilute the extracellular volume. To handle these problems, dialysis was carried out. The indications which make one lean toward peritoneal or hemodialysis depend on multiple factors, but in this case the critical factor was the relative effects of the two techniques in terms of the manipulation of the patient's water volumes and total solute concentration. Peritoneal dialysis in this patient would have exposed him to a relatively dilute solution of a normal osmolarity. This would have produced osmotic movements of water into

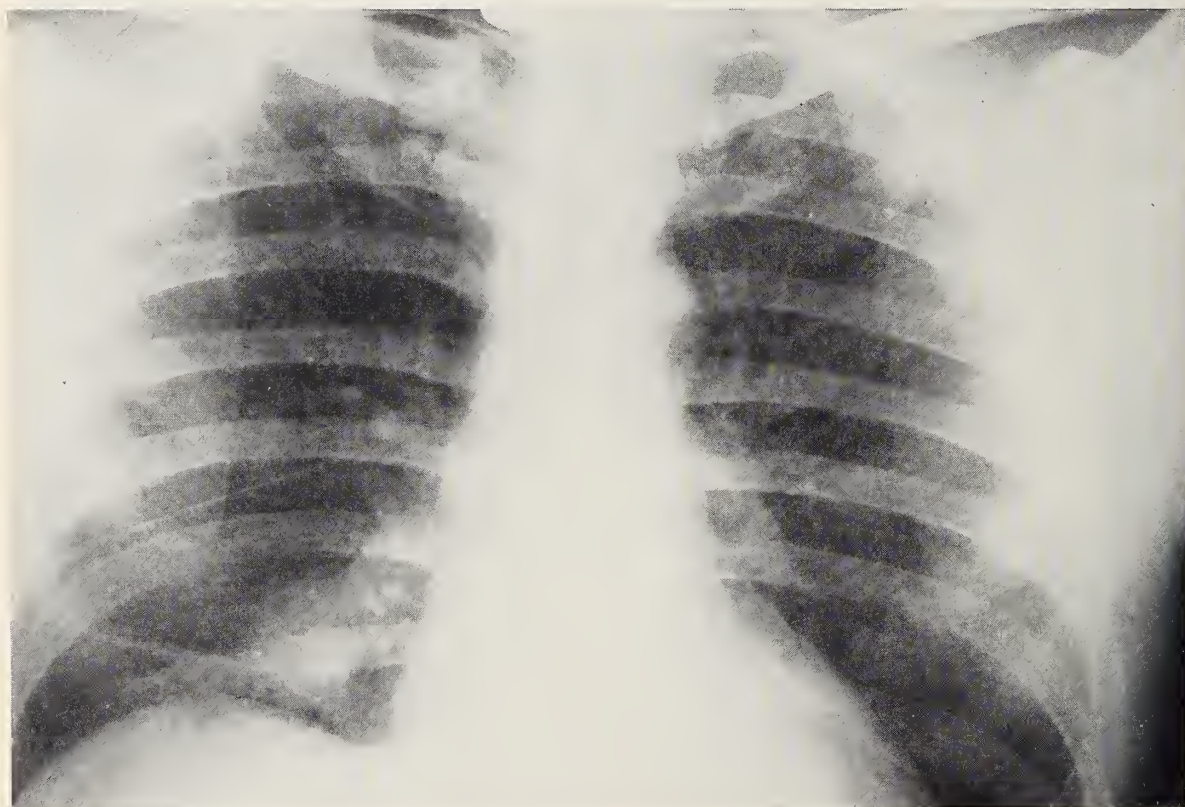


Figure 2.—X-ray film taken five days later after admission. Note lesion at right base.



the extracellular fluid volume, which would have been an undesirable effect, producing further expansion of the already increased volume of extracellular fluid. To dilute the patient's intracellular fluid and at the same time remove the excess extracellular fluid volume, hemodialysis at normal osmolarity but under increased pressure was undertaken. Dr. George Duffy will describe the patient's response to this form of therapy.

DR. MAURICE SOKOLOW:\* Dr. Gulyassy, when you began your discussion of the present case, you indicated that you would turn later to a more general dissertation on the treatment of acute renal failure.

DR. GULYASSY: Because of the numerous pathophysiologic complexities the disease entails, it may be most profitable for purposes of general discussion to focus on certain aspects of therapy. One aspect of the problem of acute renal failure is the attempt made to arrest the process which often occurs before our eyes. This is probably the most frustrating aspect of the treatment of acute renal failure because, as in this patient, the precise pathogenesis of the renal injury is not at all clear. We attempt to restore blood volume where there is a possibility of hypovolemia and shock contributing to the onset of acute renal failure. Beyond this, little can be done to block the evolution of incipient renal injury. Therefore, it is not surprising that physicians over the years have attempted various measures which block the development of frequently lethal acute renal failure. In recent years the most widely publicized and misunderstood attempt at the prevention of acute renal failure has been the application of osmotic diuretic agents to sustain urine flow when the output is decreasing sharply, presumably due to a decrease in the circulation of blood to the kidneys. This is an extremely complicated subject and I will limit myself to a discussion of, first, those instances where osmotic diuresis is undoubtedly a very useful therapeutic maneuver; second, those instances in which the value is perhaps doubtful, but because of the urgency of the situation the therapy may be attempted; and third, and most important of all, the fact that this is not entirely a harmless procedure.

Turning to the first point, osmotic diuretic agents, particularly urea and sucrose, have been

used since the 1930's. Currently mannitol has been most commonly used for this purpose. There are certain clear-cut situations where there is a very sound reason for using this approach. One such situation is the sudden appearance of pronounced uricosuria. Patients who are treated with chemotherapeutic agents, where there is rapid lysis of cells, often have a burst of uric acid excretion which reaches enormous proportions. In these patients, we are dealing with a simple problem of chemical solubility. Because of the very poor solubility of this compound, crystallization will occur if the volume of urine is reduced, followed by obstruction either outside the renal parenchyma or diffusely within the renal tubules. Therefore, the maintenance of high rates of urine flow will maintain the uric acid in a soluble form and abort mechanical precipitation of uric acid nephropathy.

A similar situation is massive hemolysis with the excretion of large quantities of hemoglobin. Here a similar physical consideration applies. We assume that by maintaining a brisk rate of urine output to keep the concentration of a coagulable protein at minimal levels, particularly in the distal nephron, precipitation and permanent obstruction throughout the kidney may be aborted.

A third situation in which osmotic diuresis may be indicated is prolonged cross-clamping of the aorta below the renal artery. The evidence as to the magnitude of the efficacy of mannitol here is not at all clear, nor is it clear whether other measures would not be as effective. Reported studies have shown that with the maintenance of urinary excretion before aortic cross-clamping, the incidence of oliguria after the clamping is done is certainly greatly diminished, and retrospective analysis indicates that the incidence of severe acute renal failure is also diminished.

Finally, there are certain situations in which the usefulness of the maintenance of diuresis for increasing urinary excretion and clearance of certain compounds is being evaluated. One such situation, which Dr. Frank Gotch has described in detail, is the use of mannitol diuresis to enhance the urinary excretion of barbiturates and thereby reverse the complications of barbiturate toxicity.

Now let us consider the problem of the patient with diminishing urine output, in whom one suspects incipient renal failure. In most varieties of acute renal injury there is surprisingly little evidence that inducing osmotic diuresis is effective in preventing the development of acute renal fail-

\*Professor of Medicine.

ure. Therefore it is important to examine the other aspect of this problem, namely the hazards of using such an agent. Mannitol and other non-metabolizable polyalcohols are characterized by the fact that they distribute through the extracellular fluid space. They penetrate cells at an extremely low rate and are essentially non-reabsorbable from the filtrate in the normal kidney. If mannitol is injected into a normal person, the rising concentration as the filtrate moves down the tubule induces inhibition of sodium reabsorption, followed by diuresis which produces progressive clearance of the mannitol from the circulation. In the patient with a very limited renal excretion, the clearance of mannitol will depend upon the extremely limited extrarenal losses, which amount to approximately 5 ml per hour per kilogram of body weight. In a 70-kilogram patient this would be a net clearance of only 4 or 5 ml per minute, approximately 5 per cent of normal clearance by renal excretion. Therefore, repeated injection of this type of agent when there is no efficient route of excretion can produce progressive accumulation of the substance in plasma and extremely important disturbances in fluid and electrolyte patterns. Important histological changes, which may be related to the sudden appearance of renal failure as a secondary consequence to the administration of the osmotic agent have also been described. A striking pattern of vacuolization of the proximal tubule after injection of large quantities of glucose, sucrose or mannitol was termed "osmotic nephrosis" in the 1930's. This lesion in recent years has either been forgotten or assumed to be harmless. The present case and several similar ones, however, strongly suggest that this casual attitude is unwarranted.

DR. GEORGE DUFFY:<sup>\*1</sup> As Dr. Gulyassy has said, the only method of removing this non-metabolizable material in the case of renal shutdown is either by dialysis or, possibly, by an exchange transfusion. Hemodialysis was begun and the patient's serum sodium, which was 129 mEq per liter 15 minutes after dialysis was started, was 146 mEq after six hours of dialysis. The blood urea nitrogen fell from 116 mg per 100 ml to 56 mg. The calculated serum osmolarity was 300 milliosmoles per liter at the beginning of dialysis and 313 at the end. The osmotic gap had decreased from 117 to 37 mOsmol per liter, which was a decrease

from 2,100 mannitol of mg per 100 ml to 668 mg per 100 ml. At the end of dialysis the patient's mental status had greatly improved.

DR. SOKOLOW: Dr. Gotch, would you care to make any comment?

DR. FRANK A. GOTCH:<sup>\*2</sup> As Dr. Gulyassy pointed out, mannitol may be of value in increasing urine flow in patients with transfusion reactions, acute hemolysis and acute hyperuricemia. Based on our experience in barbiturate ingestions, a loading dose of about 1 gm of mannitol per kilogram of body weight should initiate an osmotic diuresis of 300 to 500 ml per hour. Subsequent maintenance of mannitol to sustain the osmotic diuresis at this level will generally amount to about 0.5 gm of mannitol per kg of body weight per hour. It is important to note that the maximum concentration of mannitol achieved in the urine is about 350 milliosmoles per kg, or 5 per cent mannitol. Therefore, if 20 per cent mannitol is used, the urine volume must be at least four times the infused mannitol volume or there will be predictable accumulation of mannitol in the plasma. If 5 per cent mannitol is used, the urine volume should at least equal the mannitol volume.

#### EDITOR'S FOLLOW-UP NOTE:

Following presentation at these rounds, the patient was transferred to the surgical service where right pneumonectomy was performed for a bronchogenic carcinoma of the right lower lobe. The postoperative course was uncomplicated and on the day of discharge from the hospital the serum creatinine was 1.4 mg per 100 ml.

Generic and Trade Name of Drug.  
Diphenylhydantoin—*Dilantin*.

#### ACUTE RENAL FAILURE

##### Recent Summaries in the Literature

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<sup>\*1</sup>Intern in the Department of Medicine.

<sup>\*2</sup>Associate Clinical Professor of Medicine.



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**California  
Medicine**

## EDITORIAL

### Annual Session, 1966

AT ITS 95TH ANNUAL MEETING the CMA dealt extensively with matters having a bearing on the operation of government-sponsored medical care plans, adopted statements of attitude on several pressing questions affecting public health, conducted internal business of the Association and carried out an extremely successful program of scientific meetings.

In resolutions concerned with making governmental medical care programs workable within the framework of sound medical practice, the House of Delegates:

- Expressed concern that the American people seem to be expecting more from Medicare than the plan entails and urged an educational campaign to notify them that the plan does not provide payment in full for the entire medical care for those who are covered, without exclusions or "deductibles."

- Asked that the Medicare legislation be amended to permit a patient to be paid on presentation of the physician's bill rather than a *receipted* bill. This would help to maintain the patient's normal pecuniary role in the physician-patient relationship and to forestall the possible development of a system under which the patient abandoned his position as the buyer of a service and let the business of medical care and the payment for it become a transaction between the physician and a governmental agency.

- Voted to ask the American Medical Association to bring to the attention of appropriate federal agencies the responsibility of government hospitals for establishing active utilization review

committees such as those required in hospitals in which patients are treated under Medicare.

- Resolved that California Medical Association representatives and CMA-associated organizations use "usual, customary and reasonable" fees as the basis for negotiation of contracts or agreements involving payment for physician's services.

- Reassured physicians that hospital medical staffs and their committees are responsible solely to their medical staffs and not to government or other outside agencies.

Four resolutions took up questions in which there has been growing public interest in recent years. On these issues the House of Delegates acted as follows:

- Supported the concept of medically justifiable abortion, taking into consideration the health of both the mother and the product of conception, and recommended that legislation to this end should provide proper medical control through established hospital staffs or component medical society committees.

- Referred to the Council for further study a resolution urging the State Legislature to reclassify marijuana from a "narcotic drug" to a "dangerous drug" and that the CMA study narcotics and dangerous drugs with the aim of revising present laws and their enforcement where advisable.

- Approved the support and encouragement of "implied consent," legislation in California under which anyone receiving a driver's license in the state tacitly would assent to the extraction of a blood specimen in certain conditions when he is suspected of driving while drunk.

- Adopted a resolution that physicians be reminded of legal requirement that they report cases

of venereal disease and permit confidential interview of patients by public health personnel in the interest of controlling "the alarming increase" in the incidence of such diseases "among teenagers and young adults."

In actions concerned with the internal functions and administration of the Association, the House of Delegates:

- Voted an increase in annual dues to ninety dollars.

- Reaffirmed the section of *Guiding Principles for Physician-Hospital Relationships* that establishes a method of cooperation between medical staff and hospital administration where patient care and staff organization are involved, and requested the Joint Commission on Accreditation of Hospitals to review accreditation of hospitals where major decisions involving patient care and staff organization are made by unilateral decision of the hospital administration.

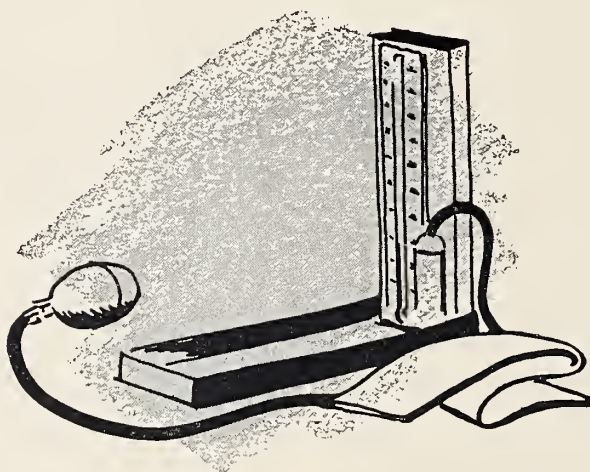
- Referred to Council for further study a proposal that CMA study in depth the feasibility of developing a program for medical care for individuals of all ages, utilizing the voluntary prepay-

ment mechanism of the private insurance industry with financial support from government to the needy on a sliding scale for premium payment.

The House of Delegates meeting was blemished late in the last day when a call for a count of members present revealed so many delegates had departed early that there was no quorum. A number of proposals for changes in the Bylaws had to be put over for action at the 1967 meeting.

On the scientific side, more than 2,700 physicians, including House of Delegates members who could spare time from their legislative duties, had spread before them a well arranged program of individual reports and panel discussions on a wide range of subjects. Guest speakers were of a quality that has come to be the hallmark of scientific sessions of the California Medical Association. Almost all meetings of scientific sections had capacity audiences and some had an overflow. In general the joint meetings of two or more sections were received with extraordinary enthusiasm.

Again the Committee on Scientific Assemblies of the Scientific Board and the officers of the Scientific Sections are to be commended for a valuable educational service to our members.





# California Medical Association



## NOTICES AND REPORTS

### Continuing Medical Education

#### Continuing Education in the Community Hospital

ALFRED W CHILDS, M.D.

*Continuing Education Committee  
Presbyterian Medical Center, San Francisco*

FURTHER DEVELOPMENT OF continuing education for physicians in California requires the movement of programs away from university centers and into the local places of work of physicians. Continuing education is most effective in the improvement of a physician's skills in care of patients when it becomes a continuous part of his daily life.<sup>3,4,5</sup> The goal of making each community hospital a teaching hospital is rapidly becoming attainable as methods of organization and financing improve and our knowledge of the processes of learning and forgetting are applied to the lifetime education of the practitioner.

Although we have extensive programs of physician education in California, we recognize serious gaps and deficiencies. According to a survey by the Ad Hoc Committee on Continuing Education of the California Medical Association,<sup>2</sup> 266 courses of continuing education offered in 1959-60 were attended by 31,276 physician enrollees—a number far greater than the total number of private practitioners in the state. But this educational activity

involving large investments of time by participants and faculty has been criticized by the Committee and others as being inefficient and having wasteful duplications and conflicts in scheduling. No one has satisfactorily evaluated these programs in relation to the day-to-day needs of physicians and the effects on the quality of patient care in the community.<sup>5,9</sup> Some have asked if programs are more often designed to satisfy needs of the sponsoring institutions than those of the participating practitioners.

Throughout the state, physicians receive a surfeit of invitations to courses; but some investigators express uneasiness that the skills of some practitioners are becoming out of date<sup>11</sup> and not all regions provide a quality of medical care approaching that available in the major centers. Analysis of the 181 courses in California listed for the current year by the Council on Medical Education of the American Medical Association provides evidence of the growth defects of continuing education of the State.<sup>1</sup> Courses are offered mostly

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in the urban medical centers: Although 44 per cent of practicing physicians are located outside Los Angeles, San Francisco and Alameda Counties, only 10 per cent of listed courses are offered outside these counties. Some subjects have excessive coverage and others none: of the 39 fields of study in the AMA classification, only 14 are represented by more than two courses in California. Teaching is short-term and not continuing: all except 40 listed courses are of the "concentrated" type, and only three postgraduate traineeships are listed.

Courses are offered at only a few medical-care institutions. Only six California institutions list more than two courses. However, local interest in development of continuing education is indicated by the fact that 14 other institutions list one or two courses. A major catalyst for improving the distribution and quality of continuing education is the California Medical Association. It is co-sponsor of postgraduate institutes and circuit courses, and it provides coordination and other services. An important new program bringing continuing education into community hospitals is the innovating medical radio conference series of the University of California Medical Center in San Francisco.

Several observers have suggested ways to make the community hospital into a teaching institution.<sup>4,7,8</sup> Glaser<sup>6</sup> suggested that hospitals, individually or in association, employ a director of medical education to organize and administer continuing education for their medical staffs. A program for cooperative exchanges of faculty, house staff and consultants on a regional basis patterned after the successful Bingham Program in Maine and Massachusetts<sup>10</sup> has been favored by framers of recent federal legislation for regional programs. These and related programs of postgraduate traineeships for practitioners, in-service education for hospital personnel foster an atmosphere for learning within the local community. Financial support for developments such as these are expected in 1966 under the National Institutes of Health Regional Medical Programs which grew out of the proposals for a national program to conquer heart disease, cancer, and stroke. Already, in San Francisco, a representative community-wide committee is being organized to develop a regional program. Although contrary to the medical tradition that continuing education should be financed entirely by the practitioners and the medical organizations,<sup>12</sup> federal grants-in-aid for education development in

regional programs will not be entirely unwelcome and may accelerate achievement of the goal of making each hospital a teaching center.

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## The Role of the Nurse in Drawing Blood For Test Purposes

The Medical Practice Act, in general, reserves to licensed physicians the right to penetrate the skin in the health care of persons.

The California Medical Association, the California Nurses' Association, and the California Hospital Association recognize the propriety of a registered nurse properly trained in intravenous technique to draw blood samples for test purposes, if done under the order of a licensed physician.

*Joint statement by the California Nurses' Association, the California Hospital Association and the California Medical Association.*



## In Memoriam

BODEN, HERBERT NEAL, Santa Ana. Died 21 December 1965, in Santa Ana, aged 57, of coronary artery disease. Graduate of the State University of Iowa College of Medicine, Iowa City, 1934. Licensed in California in 1954. Doctor Boden was a member of the Orange County Medical Association.



BRIZEE, JOHN WARREN, Anaheim. Died March 1966, aged 35. Graduate of the State University of New York College of Medicine at Syracuse, 1956. Licensed in California in 1959. Doctor Brizee was a member of the Orange County Medical Association.



BURROWS, LLOYD ALVAN, Anaheim. Died 22 October 1965, in Leeds, Utah, aged 76, of coronary artery disease. Graduate of the Chicago College of Medicine and Surgery, Illinois, 1917. Licensed in California in 1923. Doctor Burrows was a retired member of the Orange County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



CARPENTER, CHARLES MILTON, Los Angeles. Died 25 March 1966, in Los Angeles, aged 70, of coronary occlusion. Graduate of the University of Rochester School of Medicine and Dentistry, New York, 1933. Licensed in California in 1948. Doctor Carpenter was a member of the Los Angeles County Medical Association.



CLARK, J. EMMET, Oakland. Died 8 March 1966, in Oakland, aged 95, of bronchopneumonia. Graduate of the College of Physicians and Surgeons of San Francisco, 1901. Licensed in California in 1901. Doctor Clark was a retired member of the Alameda-Contra Costa Medical Association and the California Medical Association, and an associate member of the American Medical Association.



CRYST, JAMES H., Los Angeles. Died 17 March 1966, in Los Angeles, aged 69, of pulmonary emboli. Graduate of Rush Medical College, Chicago, Illinois, 1923. Licensed in California in 1923. Doctor Cryst was a member of the Los Angeles County Medical Association.



DOZIER, LINWOOD, Stockton. Died 23 March 1966, in Stockton, aged 79. Graduate of the University of California School of Medicine, Berkeley-San Francisco, 1912. Licensed in California in 1912. Doctor Dozier was a member of the San Joaquin County Medical Society.



FRASER, HUGH MILLER, Oakland. Died 20 March 1966, in Oakland, aged 81, of heart disease. Graduate of the American School of Osteopathy, Kirksville, Missouri,

1906. Licensed in California in 1918. M.D. degree from California College of Medicine, 1962. Doctor Fraser was a member of the Alameda-Contra Costa Medical Association.



HEILIGMAN, RAYMOND, Orange. Died 30 December 1965, in Orange, aged 56, of arteriosclerotic heart disease. Graduate of Jefferson Medical College of Philadelphia, Pennsylvania, 1936. Licensed in California in 1946. Doctor Heiligman was a member of the Orange County Medical Association.



HUMPHREY, NORTON R., Riverside. Died 1 February 1966, aged 52. Graduate of Marquette University School of Medicine, Milwaukee, Wisconsin, 1939. Licensed in California in 1944. Doctor Humphrey was a member of the Riverside County Medical Association.



JOHNSON, ROBERT HILDING, Berkeley. Died 9 March 1966, in Orinda, aged 51, of ventricular fibrillation. Graduate of Temple University School of Medicine, Philadelphia, Pennsylvania, 1940. Licensed in California in 1949. Doctor Johnson was a member of the Alameda-Contra Costa Medical Association.



KNERLER, CHARLES W., Los Angeles. Died 10 March 1966, in Los Angeles, aged 53, of heart disease. Graduate of the University of Michigan Medical School, Ann Arbor, 1936. Licensed in California in 1946. Doctor Knerler was a member of the Los Angeles County Medical Association.



LEWIS, CHARLES HAROLD, Corona Del Mar. Died 30 March 1966, in Corona Del Mar, aged 70, of heart disease. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1920. Licensed in California in 1920. Doctor Lewis was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



MANN, HARRY HERBERT, Los Angeles. Died 22 January 1966, in Los Angeles, of myocardial infarction. Graduate of the State University of Iowa College of Medicine, Iowa City, 1908. Licensed in California in 1913. Doctor Mann was a member of the Los Angeles County Medical Association.



MASON, BURGESS BELKNAP, Laguna Beach. Died 27 January 1966, in Laguna Beach, aged 80, of heart disease. Graduate of the University Medical College of Kansas City, Missouri, 1908. Licensed in California in 1921. Doctor Mason was a member of the Orange County Medical Association.

MCGEE, JOHN W., Los Angeles. Died 12 March 1966, in Los Angeles, aged 57. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1939. Licensed in California in 1939. M.D. degree from California College of Medicine, 1962. Doctor McGee was a member of the Los Angeles County Medical Association.



NIELSON, JOSEPH L. JR., Whittier. Died 17 February 1966, in Whittier, aged 50, of heart disease. Graduate of the University of Southern California School of Medicine, Los Angeles, 1942. Licensed in California in 1943. Doctor Nielson was a member of the Los Angeles County Medical Association.



REYNOLDS, T. GORDON, Loma Linda. Died 7 March 1966, in Loma Linda, aged 69. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1923. Licensed in California in 1923. Doctor Reynolds was a member of the Los Angeles County Medical Association.

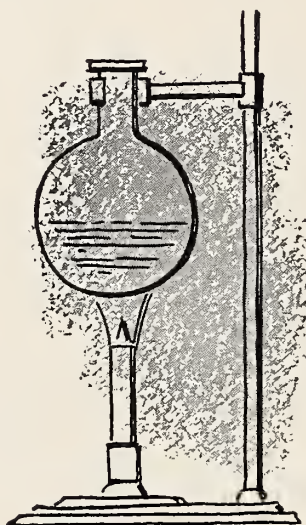
SCHERR, PETER JOSEPH, La Mirada. Died 8 March 1966, in Canoga Park, aged 66, of cerebral vascular accident. Graduate of the St. Louis University School of Medicine, Missouri, 1926. Licensed in California in 1941. Doctor Scherr was a member of the Los Angeles County Medical Association.



SMALLEY, J. WARNER, Stockton. Died 12 March 1966 in Stockton, aged 55. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1933. Licensed in California in 1933. M.D. degree from California College of Medicine, 1962. Doctor Smalley was a member of the San Joaquin County Medical Society.



TWAY, LAWRENCE EDWARD, Los Angeles. Died 14 February 1966, in Los Angeles, aged 45, of lymphoma of the mediastinal region. Graduate of George Washington University School of Medicine, Washington, D.C., 1949. Licensed in California in 1950. Doctor Tway was a member of the Los Angeles County Medical Association.





# *16th annual regional postgraduate institute*

HARVEY'S  
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## SACRAMENTO VALLEY COUNTIES

Presented cooperatively by Sacramento Valley Counties Medical Societies, Stanford University School of Medicine, and the Committee on Continuing Medical Education, California Medical Association.

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All California Medical Association members and their families are cordially invited to attend.

## THE TOOLS OF TREATMENT

### PROGRAM

#### THURSDAY, JUNE 23

##### *Afternoon Session*

- 1:15—Welcome—Orrin Cook, M.D.
- 1:30—The Perils of Zealous Treatment—Surgical, Roy Cohn, M.D.; Medical, William P. Creger, M.D.
- 2:30—Blood and Blood Products, "To Give or Not to Give"—William P. Creger, M.D.

- 3:15—PANEL DISCUSSIONS AND CONCURRENT WORKSHOPS (you may go to one of your choice):

##### PANEL DISCUSSIONS

- A. Diseases of Medical Progress—Moderator: Fred Sobeck, M.D.

Panel: William G. Bush, M.D., Roy Cohn, M.D., Calvin R. O'Kane, M.D., Philip J. Reilly, M.D.

- B. Use of Blood and Blood Products—Moderator: Robert Edmondson, M.D.

Panel: James A. Affleck, M.D., James C. Bramham, Jr., M.D., William P. Creger, M.D., Paul G. Hattersley, M.D., Edward A. Smeloff, M.D.

CONCURRENT WORKSHOPS (limited to 20 each by advance sign-up)

- A. Injuries to the Hand, Immediate Care and Long-Term Results.

Chairman: Roy L. O'Neal, M.D.

Panel: Robert A. Chase, M.D., Andrew M. Hazen, M.D.

- B. Newer Methods of Control of Infection in the Urinary Tract.

Chairman: James A. Klinefelter, M.D.

Panel: Curtis H. McDonnell, M.D., Thomas Stamey, M.D.

#### FRIDAY, JUNE 24

##### *Morning Session*

- 9:00—Angiography: Recent Advances in Technique and Application in New Fields—Ingmar Wickbom, M.D.

- 9:45—Clinical Uses of Chromosome Studies—Luigi Luzzatti, M.D.

- 10:45—PANEL DISCUSSIONS (you may go to one of your choice):

- A. New Diagnostic Techniques in Radiology—Moderator: Rob H. Kirkpatrick, M.D.

Panel: Dixon L. Hughes, M.D., Harold Lowe, M.D., Ivan D. Siddons, M.D., Ingmar Wickbom, M.D.

- B. Clinical Uses of Chromosome Studies—Moderator: Charles M. Blumenfeld, M.D.

Panel: Mark A. Dentinger, M.D., Luigi Luzzatti, M.D., Dennis M. Marks, M.D.

12:00—Luncheon

**Trends in Medical Education**—Robert J. Glaser, M.D., Vice President for Medical Affairs and Dean, Stanford University School of Medicine

*Afternoon Session*

2:00—"Odd-ball Diseases"—**Relationship of Hypersensitivity to Immunologic Diseases and Protective Immunity**—Sidney Raffel, M.D.

3:15—CONCURRENT WORKSHOPS (you may go to one of your choice—limited to 30 each by advance signup):

A. **Injuries to the Face**—Quentin Bonser, M.D., Chairman, Robert A. Chase, M.D., Robert M. Faggella, Jr., M.D.

B. **Care of the Premature Child**—Peter A. Michaels, M.D., Chairman, Philip Sunshine, M.D., Frederick N. Fisher, M.D.

C. **Clinical Problems in the Diagnosis and Treatment of Pancreatitis**—Seymour Bradus, M.D., Chairman, Harry Oberhelman, Jr., M.D., Paul R. Sharick, M.D.

SATURDAY, JUNE 25

*Morning Session*

9:00—**Newer Antibiotics, Clinical Uses and Experiences**—Harold J. Simon, M.D.

9:45—**Regional Enteritis and Ulcerative Colitis, Results of Current Therapy**—Keith B. Taylor, M.D.

10:45—PANEL DISCUSSIONS (you may go to one of your choice)

A. **Therapy with Newer Antibiotics**—Moderator: Cameron Ward, M.D.

Panel: Walton K. Brainerd, M.D., E. T. Rulison, Jr., M.D., Harold J. Simon, M.D., William J. Whalen, M.D.

B. **Regional Enteritis and Ulcerative Colitis**—Moderator: Frederick A. Schroeder, M.D.

Panel: Keith B. Taylor, M.D., J. Romelyn Warburton, M.D., Donald S. Weaver, M.D.





# NEWS & NOTES

NATIONAL • STATE • COUNTY

## ALAMEDA

Dr. Irving R. Tabershaw, professor of occupational medicine and head of the Office of Environmental Health and Safety at the University of California, Berkeley, has been named to a five-year term on the board of directors of the Industrial Medical Association.

## LOS ANGELES

At the 42nd annual meeting of the Western Section of the American Urological Association held in Portland, April 17-21, Dr. John W. Dorsey of Long Beach was elected president, Dr. Carl E. Burkland of Sacramento, president-elect, and Dr. Earl F. Nation, Pasadena, secretary-treasurer.

\* \* \*

The University of California, California College of Medicine, has announced the following appointments to the faculty:

Anesthesiology—Garó H. Kodjahabian, M.D., and Claire M. Stiles, M.D. as clinical instructors.

Gynecology and Obstetrics—Theodore J. Bersentes, M.D., assistant research gynecologist.

Medicine—William Patrick Murphy, M.D., clinical instructor, and Russell L. Poucher, M.D., lecturer.

Ophthalmology—Dale H. Hauck, M.D., associate clinical professor, and George K. Kambara, M.D., clinical professor.

Orthopedic Surgery—Leon L. Wiltse, M.D., assistant clinical professor.

Pediatrics—Susie W. Fong, M.D., assistant professor.

\* \* \*

The Shock Research Unit of the USC School of Medicine has announced that it is offering an advanced fellowship in clinical physiology to physicians who have completed residency training in internal medicine, surgery or anesthesiology. The program is centered in the USC Shock Research Unit at the Los Angeles County Hospital. It emphasizes investigations on hemodynamic, respiratory, and metabolic defects in critically ill patients, both at the bedside and in the experimental laboratory. Experience in the application of computer techniques, statistical methods, and radioisotopic measurements to clinical investigation and practice is also provided.

Inquiries may be addressed to the Director, Shock Research Unit, USC School of Medicine, Los Angeles 90033.

Dr. Matthew N. Hosmer of San Francisco, who retired as Secretary of the California Medical Association at the Annual Session in March, was presented with a plaque citing him for outstanding service during the seven years he served in that position.

Dr. Helen B. Weyranch of San Francisco was appointed by the Council to the post vacated by Dr. Hosmer.

## PLACER-NEVADA

The first scholarship fund for the new School of Medicine at the University of California, Davis, has been presented by the Placer-Nevada Medical Society.

The presentation of the more than \$16,000 was made April 13 to Dean Charles John Tupper by Dr. Bruce Becker, president of the society, at its meeting in Roseville.

The fund will be used for scholarships or loans for medical students in the new school planned to open at Davis in 1968.

Dr. Tupper in receiving the gift expressed his great satisfaction with this concrete evidence of the continuing interest and support that organized medicine gives to medical education.

\* \* \*

Dr. Richard Wilbur, Palo Alto, was elected chairman of the Board of Trustees of the California Physicians' Service at its meeting March 30 in San Francisco. Dr. Milo Youel of San Diego was elected vice chairman, Dr. Wilbur Rogers, Glendale, secretary, and Dr. Bert Halter, San Francisco, treasurer.

Dr. Wilbur replaces Dr. William H. Thompson, San Mateo, who will serve as an ex officio member of the board for one year.

\* \* \*

A National Conference on Infant Mortality, sponsored by the American Medical Association's Committee on Maternal and Child Care, will be held on August 12-13 at the Fairmont Hotel in San Francisco.

An invitation to attend is being extended to chairmen and members of all state and county maternal and child care and perinatal and maternal mortality committees, state health department director of maternal and child health, medical school faculty members in departments of obstetrics and gynecology, pediatrics, and preventive medicine, and other interested physicians and representatives of groups concerned with the problems of infant mortality.

The program has been planned to explore effective approaches for continuing the reduction of infant mortality. Further information about registration may be obtained by addressing: Secretary, Committee on Maternal and Child Care, 535 North Dearborn Street, Chicago 60610.

# EDUCATION NOTICES

## Meetings and Courses

### COMMITTEE ON CONTINUING MEDICAL EDUCATION

THIS BULLETIN of the dates of continuing education programs and the meetings of various medical organizations in California is supplied by the Committee on Continuing Medical Education of the California Medical Association. In order that they may be listed here, please send communications relating to your future meetings or postgraduate courses to Committee on Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco, California 94102.

#### KEY TO ABBREVIATIONS AND SYMBOLS

##### Medical Centers and CMA Contacts for Postgraduate Course Information

<b>CMA:</b>	<b>California Medical Association</b> For information contact: Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco 94102. PRospect 6-9400, Ext. 68.
<b>LLU:</b>	<b>Loma Linda University</b> For information contact: W. F. Norwood, Ph.D., Associate Dean, Continuing Education, Loma Linda University School of Medicine, 1720 Brooklyn Ave., Los Angeles 90033, ANgeles 9-7241, Ext. 214.
<b>PRES. MED. CTR.</b>	<b>Presbyterian Medical Center</b> For information contact: Arthur Selzer, M.D., chairman, Education Committee, Presbyterian Medical Center, Clay and Webster Streets, San Francisco 94115. WEst 1-8000.
<b>UCLA:</b>	<b>University of California at Los Angeles</b> For information contact: Donald Brayton, M.D., Assistant Dean for Postgraduate Medical Education, 15-39 Rehabilitation Center, University of California Center for Health Sciences, Los Angeles 90024, 478-9711, Ext. 4345.
<b>UCSF:</b>	<b>University of California, San Francisco</b> For information contact: Seymour M. Farber, M.D., Dean, Educational Services and Director, Continuing Education, University of California Medical Center, Room 565-U, San Francisco 94122, 666-1692.
<b>USC:</b>	<b>University of Southern California</b> For information contact: Phil R. Manning, M.D., Associate Dean, Postgraduate Division, USC School of Medicine, 2025 Zonal Ave., Los Angeles 90033, Capital 5-1511, Ext. 300.
<b>STAN:</b>	<b>Stanford University</b> For information contact: Roy Cohn, M.D., Associate Dean for Graduate Affairs, Stanford University School of Medicine, 300 Pasteur Drive, Palo Alto, DAVenport 1-1200.

### MAY

May 16-18—**National Biomedical Instrumentation Symposium.** Sponsored by Instrument Society of America. Disneyland Hotel, Anaheim. Monday-Wednesday. \$20: members of ISA or AMA, \$25: others. Contact: Thomas B. Weber, M.D., Beckman Instruments, Inc., 2500 Harbor Blvd., Fullerton.

May 17—**Southern California Medical Television Network:** "The Clinician's Evaluation of Pulmonary Function." Produced by USC School of Medicine and The Tuberculosis and Health Association. Station KCET. Tuesday. 8:00 to 9:00 a.m. For list of participating hospitals contact UCLA.

May 18—**Annual Symposium of the Medical Staff of the Memorial Hospital of Long Beach.** Memorial Hospital, 2801 Atlantic Avenue, Long Beach. Wednesday at 1:00 p.m. Contact: S. Ede, M.D., secretary, Medical Symposium Committee, MHLB.

May 18—**Peripheral Vascular Disease.** USC. Wednesday. 7 hours.

May 19—**California Heart Association Annual Scientific Session.** Ambassador Hotel, Los Angeles. Thursday. 6 hours. No fee. Contact: Arthur Feinfeld, M.D., CHA, 1370 Mission Street, San Francisco.

May 20-21—**San Diego Academy of General Practice Annual Postgraduate Symposium presented in cooperation with University of Oregon School of Medicine.** Vacation Village Hotel, Mission Bay, San Diego. Friday-Saturday. Contact: Orlando P. Johann, M.D. 731 E. Broadway, El Cajon.

May 20-21—**Pain.** UCSF. Friday-Saturday. \$40. 10½ hours.

May 21—"Clinic Day"—**Diseases of Medical Progress.** Channing House Auditorium, Palo Alto. Saturday. 9:00 a.m. to 3:30 p.m. Contact: R. Hewlett Lee, M.D., Palo Alto Medical Clinic, 300 Homer, Palo Alto.

May 23-25—**American Thoracic Society Annual Meeting.** Hilton Hotel, San Francisco. Monday-Wednesday. Contact: James Kieran, M.D., chairman, Medical Sessions Committee, American Thoracic Society, 1790 Broadway, New York, N.Y. 10019.

May 24—**Southern California Medical Television Network:** "Chronic Diseases of the Liver." Produced by UCLA (Los Angeles County Harbor General Hospital). Station KCET. Tuesday. 8:00 to 9:00 a.m. For list of participating hospitals contact UCLA.

May 28-June 29—**Medical Centers of Europe.** USC. 50 hours. \$250.

May 31—**Southern California Medical Television Network:** "What's New in Cancer." Produced by Pres. Med. Ctr. and Childrens Hospital, San Francisco. Station KCET. Tuesday. 8:00 to 9:00 a.m. For list of participating hospitals contact UCLA.

### JUNE

June 2—**Symposium on Diet and Coronary Heart Disease.** Colonial Room, St. Francis Hotel, San Francisco. Thursday. 8:30 a.m. to 4:00 p.m. Contact: Mrs. Helen Fung, San Francisco Heart Association, 259 Geary Street, Room 300, San Francisco 94102.

June 10-11—**Convulsive Disorders.** UCSF. Friday-Saturday. 12 hours. \$40.

June 11-12—**The Drug Takers.** UCLA. Saturday-Sunday. 12 hours. \$15.



June 11-12—**Orthopaedic Problems in the Adult.** Lebanon Hall, Cedars of Lebanon Hospital Division, 4822 Fountain Avenue, Los Angeles. Saturday-Sunday. \$15. Contact: Alex Evelove, director, Cedars-Sinai Medical Center, 8720 Beverly Blvd., Los Angeles 90048.

June 16-19—**California Society of Anesthesiologists Biennial Scientific Meeting.** Sahara Tahoe Hotel, South Shore, Lake Tahoe. Thursday-Sunday. \$25. Contact: Mr. Norman R. Catron, executive secretary, CSA, 39 North San Mateo Drive, San Mateo 94401.

June 17—**Attending Staff Association of Olive View Hospital Symposium on Infectious Diseases.** OVH, Olive View. Friday. Contact: Joseph K. Indenbaum, M.D., secretary-treasurer, ASAOVH, Olive View.

June 18—**Diagnosis and Management of Infectious Diseases.** Amphitheater Conference Room, Children's Hospital of Orange County, 1109 W. La Veta, Orange 92666. Saturday. 8:30 a.m. to 4:00 p.m. \$5 (lunch included). Contact: Merl J. Carson, M.D., Medical Director, CHOC.

June 22-24—**Highlights of Modern Ophthalmology.** Lions Eye Bank. Wednesday-Friday. 8 hours daily. \$75. Contact: Eva del Oro, secretary, Lions Eye Bank, 2018 Webster Street, San Francisco.

June 22-24—**Treatment of Fractures.** USC. Wednesday-Friday.

June 23-25—**SACRAMENTO VALLEY COUNTIES—Regional Postgraduate Institute presented by California Medical Association in cooperation with Stanford.** Harvey's Resort Hotel, Lake Tahoe. Thursday noon-Saturday noon. \$15. "Advances in Therapy: Diseases of Medical Progress, Newer Antibiotics, Peptic Ulcer Disease, Cosmetic Plastic Surgery." Chairman: John N. Miller, Jr., M.D., 5301 F Street, Sacramento.

## JULY

July 2-6—**Seminars for General Practitioners.** UCLA at Lake Arrowhead. Saturday-Wednesday. 18 hours. \$110.

July 10-12—**Hospital Infections Control.** Neuropsychiatric Institute Auditorium, 720 Westwood Plaza Bldg., No. C-18-183, West Los Angeles. Sunday-Tuesday. Contact: John W. Brown, M.D., Bureau of Communicable Diseases, Department of Public Health, 2151 Berkeley Way, Berkeley 94704.

## AUGUST

August 7-10—**Advanced Seminars in Pediatrics.** "Immunologic Principles and Their Clinical Applications." UCLA at Lake Arrowhead. Sunday-Wednesday. 15 hours. \$110.

August 13-14—**Obstetrics and Gynecology.** UCLA. Saturday-Sunday. 16 hours.

August 17-21—**Advanced Seminars in Dermatology.** UCLA at Lake Arrowhead. Wednesday-Sunday. 15 hours.

August 21-24—**Advanced Seminars in Internal Medicine.** UCLA at Lake Arrowhead. Sunday-Wednesday. 15 hours. \$110.

August 28—**American Association of Electromyography and Electrodiagnosis.** Sheraton-Palace Hotel, San

Francisco. Sunday. Contact: Max Karl Newman, M.D., director, 16861 Wyoming Avenue, Detroit 48221.

August 28-31—**Medicine and Religion.** UCLA at Lake Arrowhead. Sunday-Wednesday. 15 hours.

August 28-September 2—**American Academy of Physical Medicine and Rehabilitation.** Sheraton-Palace Hotel, San Francisco. Sunday-Friday. Contact: Harriet E. Gillette, M.D., secretary, Cleveland Clinic, Cleveland.

## SEPTEMBER

September 8-10—**Saint John's Hospital Annual Postgraduate Assembly.** SJH, 1328 22nd Street, Santa Monica. Thursday-Saturday. Contact: John C. Eagan, M.D., director, SJH.

September 14-16—**Hospital Infections Control.** Auditorium, Medical Sciences Bldg., UCSF. Wednesday-Friday. Contact: John W. Brown, M.D., Bureau of Communicable Diseases, Department of Public Health, 2151 Berkeley Way, Berkeley 94704.

September 15-16—**Merritt Hospital Medical Seminar.** Claremont Hotel, Berkeley. Thursday-Friday. 10 hours. Contact: Robert R. Crosbie, M.D., secretary of the Staff, MH, Hawthorne and Webster, Oakland.

September 16-17—**Advances in Electrocardiography.** Sponsored by Daniel Freeman Hospital, 333 N. Prairie Ave., Inglewood. To be held at the Statler Hotel and Los Angeles County Medical Association Bldg., Los Angeles. Friday-Saturday. 10 hours. \$15 members, \$25 non-members. Contact: W. Graf, M.D., chairman, 3701 Stocker Street, Los Angeles 90008.

September 17—**Annual Symposium on Cardiovascular Disease.** Sponsored by the Santa Barbara County Heart Association. Biltmore Hotel, Santa Barbara. Saturday. 6 hours. \$12.50. Contact: Sara Clyde, executive director, 18 La Arcada Court, Santa Barbara.

September 25-26—**Annual San Francisco Cancer Symposium.** "High Energy Electrons in the Treatment of Cancer." Sponsored by Claire Zellerbach Saroni Memorial Tumor Institute. Sunday-Monday. 10 hours. \$25. Contact: Jerome M. Vaeth, M.D., director, STI.

September 26—**Society for Pediatric Radiology.** Hilton Hotel, San Francisco. Monday. Contact: John L. Gwinn, M.D., treasurer, Children's Hospital, 4614 Sunset Blvd., Los Angeles 90027.

September 27-30—**American Roentgen Ray Society.** Hilton Hotel, San Francisco. Tuesday-Friday. Contact: C. Allen Good, M.D., executive secretary, Mayo Clinic, 200 First Street, SW, Rochester, Minn. 55901.

September 28-29—**Los Angeles County Heart Association Annual Symposium on Heart Disease.** Statler Hilton Hotel, Los Angeles. Wednesday-Thursday. 12 hours. Contact: Professional Symposium Committee, 2405 West Eighth Street, Los Angeles 90057.

September 28-30—**Annual Postgraduate Symposium on Heart Disease.** Sponsored by San Francisco Heart Association. St. Francis Hotel, San Francisco. Wednesday-Friday. 18 hours. \$35. Contact: Gene C. Taylor, executive director, SFHA, 259 Geary Street, San Francisco.

September 28-30—**American Association of Medical Clinics.** Hotel Del Coronado, San Diego. Wednesday-Friday. Contact: Edwin P. Jordan, M.D., executive director, P.O. Box 58, Charlottesville, Va. 22902.

## OCTOBER

October 8-9—**Recent Developments in Nuclear Medicine.** UCLA. Saturday-Sunday. 16 hours.

September 30-October 1—**Annual Professional Symposium on Heart Disease.** Town and Country Hotel, San Diego. Friday-Saturday. 10 hours. \$5. Contact: James E. Lasry, M.D., chairman, 3545 Fourth Avenue, San Diego 92103.

October 1—**Shufelt Society of Santa Clara County Fall Seminar.** Obstetrics and Gynecology. Auditorium, Santa Clara County Administration Bldg., 70 West Hedding Street, San Jose. \$15. Contact: H. W. Christopher, M.D., secretary, 621 E. Campbell Avenue, Campbell.

October 11—**Northeastern California Chapter of the Arthritis Foundation Symposium.** Mercy Hospital, Sacramento. Tuesday. Contact: Harold B. Strauch, M.D., 4101 J Street, Sacramento 95819.

October 28—**Kern County General Hospital Postgraduate Conference (and Alumni Day).** KCGH, 1830 Flower Street, Bakersfield. Friday. 8 hours. Contact: George A. Paulsen, M.D., KCGH.

### Courses Offered Continuously or by Arrangement

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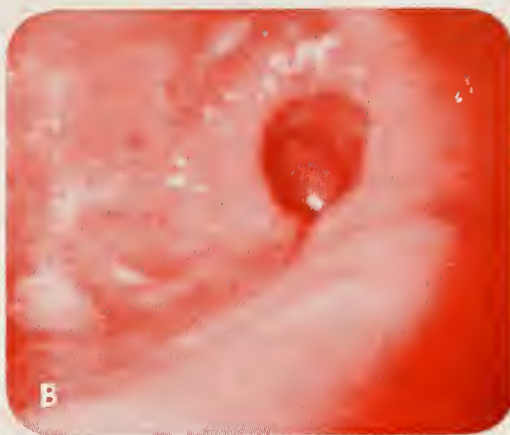
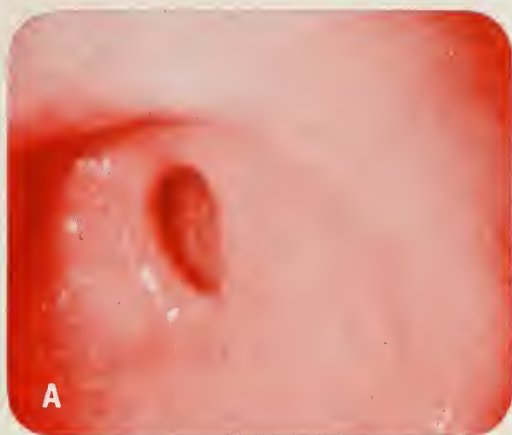
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Photographs—Harry Barowsky, M.D., Lawrence Greene, M.D., and Robert Bennett, M.D., from a Scientific Exhibit presented at the Annual Meeting of the American College of Gastroenterology, Bar Harbour, Florida, Oct. 24-27, 1965.

**SEARLE**

*Research in the Service of Medicine*

## Hechter, Godall Appointed To Biomedical Institute

(Continued from Page 32)

was a Research Fellow at the Institute for Muscle Research, Woods Hole, Mass. Before joining Boston University Physics Department in 1965, he was a Research Associate at the University of Michigan Zoology Department and Cornell University Computation Center and a member of the staff at the Research Laboratory of Electronics at Massachusetts Institute of Technology.

## Health Spending Increases; Physicians' Share Declines

Americans are increasing their spending for health care.

But they still spend more for tobacco than for hospital care, and more for cosmetics and haircuts than for doctor bills, reports *The AMA News*, published by the American Medical Association.

Spending for health care totaled \$25.2 billion in 1964, according to figures of the U.S. Department of Commerce. That's an increase of 7.8 per cent from the \$23.4 billion spent in 1963.

Hospitals receive the largest share of health-care spending—about 30 cents of every dollar. The total spent for hospital care in 1964 was \$7.6

billion. This compares with \$7.8 billion spent on tobacco products.

Other portions of the health-care dollar are divided among drugs, 17 cents; dentists, 10 cents; health insurance, 7 cents; appliances, 4 cents, and miscellaneous expenses, 5 cents.

The remaining 27 cents goes to physicians. This percentage has declined slightly over the years. Twenty years ago, physicians received about 28 cents of every dollar spent on health care.

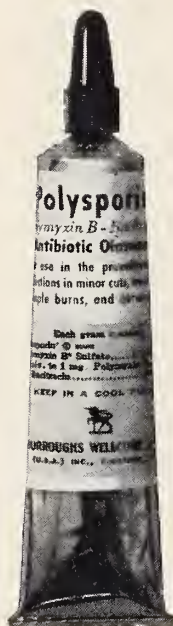
Expenditures for physicians' services totaled \$6.8 billion in 1964, compared with \$7 billion spent on personal items such as cosmetics, haircuts, and toiletries.

This was the distribution of the health-care dollar 10 years earlier: hospitals, 24 cents; physicians, 28 cents; drugs, 18 cents; dentists, 12 cents; health insurance, 8 cents; appliances, 5 cents, and other services, 5 cents.

The Department of Commerce reported these expenditures for health care in 1964:

Hospitals, \$7.6 billion, up 12.5 per cent over 1963; physicians, \$6.8 billion, up 5.5 per cent over 1963; drugs, \$4.4 billion, up 5.2 per cent; dentists, \$2.4 billion, up 5.8 per cent; health insurance, \$1.8 billion, up 6.3 per cent; appliances, \$1.1 billion, up 9.7 per cent, and other services, \$1.2 billion, up 6.9 per cent over 1963.

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## Sunscreen Mixture Doesn't Wash Off

A sunscreen lotion that doesn't wash off could be a result of research reported in a publication of the American Medical Association. The material gives sunlight protection that cannot be removed by sweating, swimming, or rubbing.

Physicians at the University of Michigan Hospital who tested the mixture say treated areas of skin in many cases resisted sunburn three times longer than untreated areas on the same persons. Of 18 persons tested, all were able to remain at least an hour in strong summer sunlight without noticeable reddening.

The mixture does not give immediate protection. It must be applied at least 12 hours before going into the sun. Persons with rashes, sores, or other forms of dermatitis cannot use the lotion.

This method for altering the built-in light filter of the skin was first reported in 1962 by two of the four physicians making this report.

The report noted that the skin's outer layer, the stratum corneum, already has some ability to block ultraviolet rays, which cause sunburning. The mixture tested produces a chemical reaction which alters the skin's filter mechanism and blocks still more of the sun's ultraviolet radiation.

The two chemicals used are dihydroxyacetone (DHA) and naphthoquinone (lawsone). Mixed with water and isopropyl alcohol, the chemicals were applied to abdominal skin of the test volunteers. In every case, their skin had been unexposed or minimally exposed to sunlight during the previous nine months.

The volunteers applied the mixture 14 to 18 hours before entering sunlight, and washed with soap and water four hours before sunbathing.

Their median reaction time—the time required to produce some skin reddening—was 33 minutes for untreated skin areas and 102 minutes for treated skin. All 18 volunteers showed reactions on unprotected skin after 60 minutes in the sunlight, but none on the protected areas.

Another mixture, using increased amounts of lawsone, was tested on four volunteers. These persons were able to tolerate up to four hours of sunlight without reddening.

Additional tests showed that more protection was given with greater amounts of the mixture and more frequent application.

Still to be perfected is a way to keep the mixed and stored chemicals stable at room temperature.

"The obvious advantage of this 'built-in' protection is that it cannot be washed off but remains until it wears off," said an editorial in the February 14 *Journal of the American Medical Association*. "Future improvement and modification of the basic compounds used in the mixture may offer advantages over available topical sun screens."

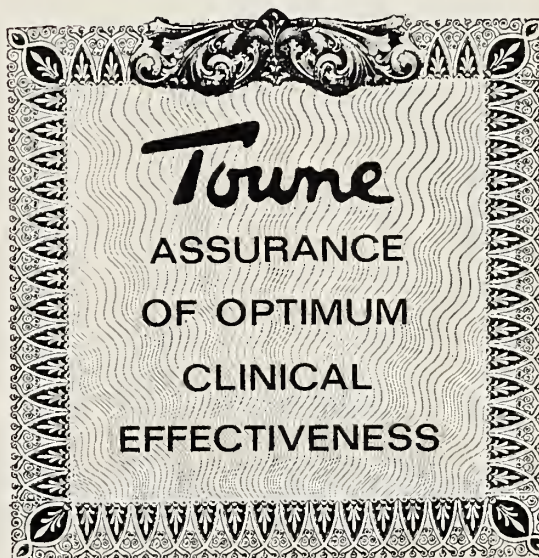
Authors of the report are Ramon S. Fusaro,

(Continued on Page 45)



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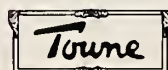


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## Sunscreen Mixture Doesn't Wash Off

(Continued from Page 37)

M.D., Walter J. Runge, M.D., Francis W. Lynch, M.D., and C. J. Watson, M.D., all of the University of Minnesota Hospital, Minneapolis. The report appeared in the January issue of the *Archives of Dermatology*, published by the AMA.

## Massive Screening For Breast Cancer

Preliminary results are encouraging in a massive x-ray screening program to detect breast cancer in women.

The February 28 *Journal of the American Medical Association* describes the cancer-detection program of the Health Insurance Plan of Greater New York and the National Cancer Institute.

Sixty thousand women between ages 40 and 64 are being examined. Thirty thousand will receive their regular medical care, and will be the control group. The remaining 30,000 are receiving medical checkups and breast x-rays three times a year.

Purpose of the study is to determine whether such a massive screening program actually does help reduce cancer deaths. Final results may not be known for five to 10 years.

Twenty-three breast cancers have been detected in the first 10,000 women examined. Sixteen of these cancers (70 per cent) were detected before they had spread to nearby lymph nodes.

Twelve of the 23 women underwent tissue examination after x-rays alone detected their cancers. In 10 cases (83 per cent), the cancers were detected before they had spread to nodal areas.

This compares with the control group, in which 14 cancers were confirmed, eight of them (57 per cent) in early stages.

Early detection alone, however, cannot decide the usefulness of the screening, a *Journal* editorial pointed out. "The final test will be whether mortality from breast cancer is reduced, and for this a 5- to 10-year follow-up is required."

Breast cancer is the leading cause of death from cancer among women in the United States.

"Despite all research and clinical efforts, there has been no significant reduction in the breast cancer death rate over the past 30 years," the editorial said. The massive screening program is "an effort that ranks high in boldness and hope," it said.

Though early findings are encouraging, they must be viewed cautiously since the survey is still in early stages, authors of the report pointed out.

They are Sam Shapiro of the Health Insurance Plan of Greater New York, Philip Strax, M.D., of the City Hospital Center at Elmhurst, Queens, N. Y., and Louis Venet, M.D., of New York Medical College and Beth Israel Medical Center, New York City.

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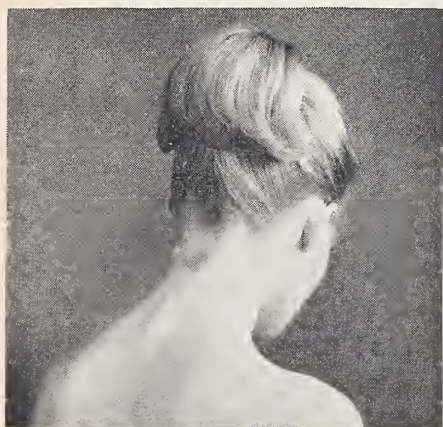
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## Medical Careers Offer Opportunity

There's a bright future for young people interested in medical service careers, says the May issue of *MD's Wife* magazine.

By the end of this decade, the health service industry may be the largest in the nation, the magazine said. There will be thousands of job opportunities for young men and women who have a sound high school background, plus some specialized training.

For men, new specialties such as inhalation therapy and nuclear medical technology offer challenging careers. Fewer than 200 certified inhalation therapists are available today; it's estimated that at least 2,000 more will be needed in the near future. These specialists assist physicians in the treatment of heart and lung ailments where life is endangered by the body's lack of oxygen.

The nuclear medical technologist works with the radioisotopes used by physicians in diagnosing and treating several diseases. Training courses for these and other specialties are being established at medical schools and hospitals throughout the country, and more are on the way.

To find out about health career possibilities, high school students should talk to their school counselor, family physician, and friends who work in medically related careers.

A young man interested in surgery recently heard of a new course being given at a surgical clinic near his home. He investigated and then enrolled in the nine-month course for operating room technicians. He learned sterile procedures, the names and uses of surgical instruments and how to set up and manage operating room equipment. Today, he has an important job assisting surgeons in a variety of delicate operations.

Girls have just as many chances for challenging careers, and are greatly needed in several jobs.

Nursing, of course, has long been high on the list of professions that offer prestige and an opportunity to serve others. In addition to registered nurses who undertake several years of intensive education and training, practical nurses are also needed to serve as part of the medical care team.

Practical nursing students train and study for approximately one year, then take state board examinations for certification to practice.

The U.S. Surgeon General's Consultant Group on Nursing sees a need for 850,000 nurses in 1970. This is about 35 per cent more than we now have.

Helping patients regain lost abilities offers work to physical therapists, occupational therapists, speech pathologists, audiologists, and technicians trained to handle special electrical equipment. Women are needed in all of these jobs.

Outside the hospital and physician's office there

(Continued on Page 16)

**cautions and adverse reactions:** The transitory drowsiness which may occur with hydroxyzine HCl usually disappears spontaneously in a few days with continued therapy, or is correctable by dosage reduction. Dryness of the mouth may be seen with higher doses. Involuntary motor activity, including rare instances of tremor and convulsions, has been reported, usually on higher than recommended dosage. Hydroxyzine HCl may potentiate barbiturates, narcotics such as meperidine, and other CNS depressants. In conjunctive use, dosage for these drugs should be decreased. Because drowsiness may occur, patients should be cautioned against driving a car or operating dangerous machinery.

**Parenteral Solution Precautions and contraindications:** This dosage form is intended only for I.M. or I.V. administration and should not under any circumstances be injected subcutaneously or intra-arterially. When the usual precautions for I.M. injection have been followed, reports of soft tissue reactions have been rare. Due to infrequent phlebitis and, rarely, reversible hemolysis or hemoglobinuria, resulting from too rapid intravenous administration of the solution, I.V. administration should be slow, no more than 25 mg. per minute, and should not exceed 100 mg. in a single dose. Particular care should be used to insure injection only into intact veins; a few instances of digital gangrene occurring distal to the injection site have been attributed to inadvertent intra-arterial injection or periarterial extravasation, both of which should be avoided. **Use in Pregnancy:** When administered to rats at high dosage, hydroxyzine induced fetal abnormalities. Until human clinical data is available adequate to establish safety in early pregnancy, hydroxyzine is contraindicated in early pregnancy. Use of hydroxyzine as an adjunct to the management of labor has been extensively reported in the literature without evidence of harm to the mother or fetus.

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## Asthma and Temperature Change

The first colder weather of fall is a bad time for asthma sufferers.

When New York City's temperature first dropped below 55 degrees last September, emergency clinic visits by asthmatics shot upward at three major city hospitals. At one hospital, visits were 195 per cent over average during the first colder days, September 25-30.

A report in a current publication of the American Medical Association shows that similar increases occurred in preceding years. The authors, however, say they do not know the cause.

Asthma attacks were not related to high pollen counts or air pollution, they said. In fact, pollen was at a relatively low level on the days of most frequent attacks.

Asthma attacks may be directly related to cold weather, or there may be an indirect relationship with some other factor, the authors said. They are Leonard Greenburg, M.D., Franklyn Field, O.D., Joseph I. Reed, M.S., of the Albert Einstein College of Medicine, Yeshiva University, and Carl L. Erhardt, Sc.D., of the New York City Department of Health. Their report appeared in the May issue of the *Archives of Environmental Health*, published by the AMA.

## Medical Careers Offer Opportunity

(Continued from Page 15)

are other opportunities for those who wish to work in medicine.

The home health aide can perform important service in homes where simple nursing care is needed. This worker usually is a mature woman who has raised her family and understands how to keep a home running smoothly. She also has special training and works under professional supervision.

There will, of course, be a continuing need for more physicians. Fourteen new medical schools are expected to be in operation within five years. These will help supply well-trained doctors to practice the increasingly complex medicine of the future.

In addition, however, there will be a need in medical research and education for university-trained specialists such as chemists, biologists, pharmacists, and mathematicians. A sound high school background in science is an important first step toward such a career.

In all, there are at least 700 different health career possibilities for young people, said *MD's Wife* magazine. Some are so new that few people have heard of them, and others are distinguished by a long tradition of service. The field of medicine offers great opportunities for young people in the years ahead, the magazine said.



## AMA Convention in Chicago June 26-30

The world's largest medical meeting, the annual convention of the American Medical Association, will be June 26-30 in Chicago.

An attendance of 45,000, including 15,000 physicians, is expected at the 115th annual meeting.

The program is outlined in a special section of the May 9 *Journal of the American Medical Association*. A diverse scientific program covering virtually every medical specialty will be presented. The AMA's policy-making House of Delegates will meet in the Palmer House Hotel and more than 350 scientific exhibits will be housed in McCormick Place convention center.

McCormick Place also will be the site of many scientific sessions and an extensive medical motion picture and television program. The telecasts will originate from the University of Illinois College of Medicine, University Hospitals, Chicago.

Charles L. Hudson, M.D., Cleveland, Ohio, will be installed as AMA president. He succeeds James Z. Appel, M.D., of Lancaster, Pa.

Topics of the six general scientific sessions include emphysema, population expansion, burns, mysterious fevers, community hospitals and coronary care units, and headaches.

Another highlight will be the Sixth Multiple Discipline Research Forum. Topics will include hematology, immunology and tumor; gastrointestinal problems; metabolism and renal diseases; neurology and pulmonary diseases, and cardiovascular subjects.

The AMA House of Delegates will convene at 3 p.m. Sunday, June 26, in Arie Crown Theater at McCormick Place. Speaker of the House is Milford O. Rouse, M.D., of Dallas, Texas.

The scientific program will open at 9 a.m. Monday, June 27, in McCormick Place. Scientific and industrial exhibits will open at 10 a.m. Sunday, June 26, in McCormick Place, and will be open Monday through Thursday, 8:30 a.m. to 5 p.m.

General registration will be in the lower lobby of McCormick Place. It will be open 10 a.m. Sunday, and from 8:30 a.m. to 5 p.m. on following days.

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## BOOKS RECEIVED

*Books received by CALIFORNIA MEDICINE are acknowledged in this column. Selections will be made for more extensive review in the interest of readers as space permits.*

### ALCOHOLIC BEVERAGES IN CLINICAL MEDICINE

—Chauncey D. Leake, Ph.D., Senior Lecturer in Pharmacology and History of Medicine, University of California School of Medicine; formerly Vice-President, University of Texas, and Director of the Medical Branch (Galveston); Past President, American Association for the Advancement of Science; and Milton Silverman, Ph.D., Director of Medical Research, Wine Advisory Board, California State Department of Agriculture; Special Consultant on Alcohol and Alcoholism, U.S. Department of Health, Education and Welfare. Year Book Medical Publishers, Inc., Chicago, Ill., 1966. 160 pages, \$4.95.

### CLINICAL OBSTETRICS AND GYNECOLOGY—Vol-

ume 9, Number 1: Radiology in Obstetrics—Edited by Alvin M. Siegler, M.D., D.Sc.; and Diseases of the Breast, edited by George C. Escher, M.D., Hoeber Medical Division (Harper & Row, Publishers, Inc.), New York, 1966. Published quarterly, \$18.00 per year, by subscription only; about 1200 pages per year.

### DRUG ADDICTION—With Special Reference to India—

R. N. Chopra, formerly Director Drug Research Laboratory, Jammu, J. & K.; and I. C. Chopra, formerly Deputy Director in charge, Regional Research Laboratory, Jammu, J. & K. Council of Scientific & Industrial Research, New Delhi, India, 1965. 264 pages, \$3.50.

### OCCUPATIONAL HEALTH OF AGRICULTURAL

WORKERS IN CALIFORNIA — State of California, Department of Public Health, Bureau of Occupational Health, December 1965. Copies are available free upon request as long as the supply lasts from the Bureau of Health Education, California State Department of Public Health, 2151 Berkeley Way, Berkeley, California 94704.

### SYMPOSIUM ON VASCULAR DISORDERS OF THE

EYE—Basic considerations in anatomy and physiology—Sponsored by The Visual Sciences Study Section, Division of Research Grants, N.I.H. (P.H.S. Conference Grant NB 05516-01 from the National Institute of Neurological Diseases and Blindness) and The Department of Ophthalmology, Presbyterian Medical Center, San Francisco. Subcommittee on vascular disorders: Jerome W. Bettman, Chairman; Raymond A. Allen; Calvin Hanna and Marie A. Jakus. Advisers to the committee: Edward W. D. Norton and Kenneth Swan. From articles appearing in the December 1965 issue of Investigative Ophthalmology. The C. V. Mosby Company, St. Louis, Mo., 1966. 186 pages, \$12.50.

### SYNOPSIS OF OBSTETRICS—Seventh Edition—Charles

E. McLennan, M.D., Professor of Gynecology and Obstetrics, Stanford University School of Medicine, Palo Alto, Calif. The C. V. Mosby Company, St. Louis, 1966. 471 pages, \$6.85.

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## NEW BOOK

**IMMUNOLOGICAL DISEASES.** Edited by Mox Somfer, M.D., et al. 966 pages. Illustrated. 1965. Little, Brown. \$30. This is an epic venture in a relatively new field. The work of 95 outstanding clinicians, it is currently the definitive volume in basic and applied immunology. A sample from the table of contents will indicate its scope: the nature of antigen and antibody combining regions, serum complement and properdin, lymphoid tissues—their morphology and roles, thymus and immunologic deficiency disease, and symptomatic treatment of otopic disorders.



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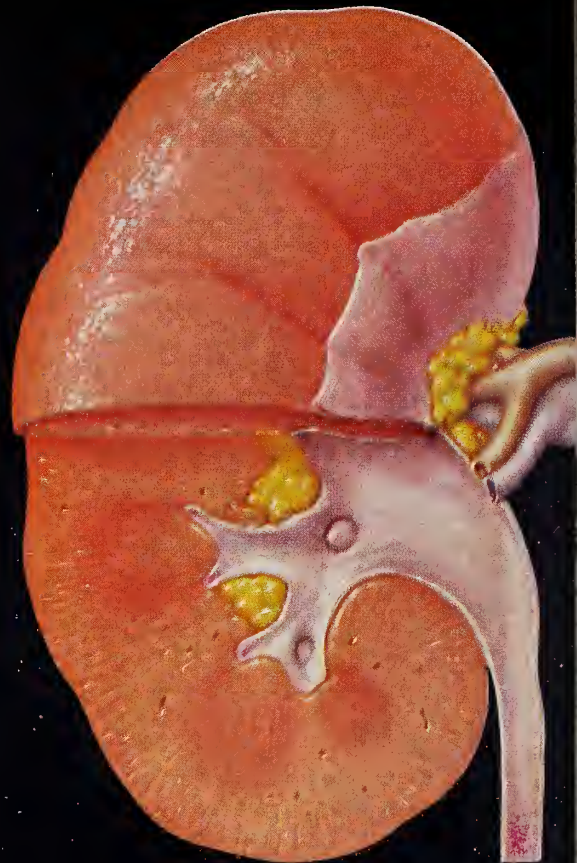
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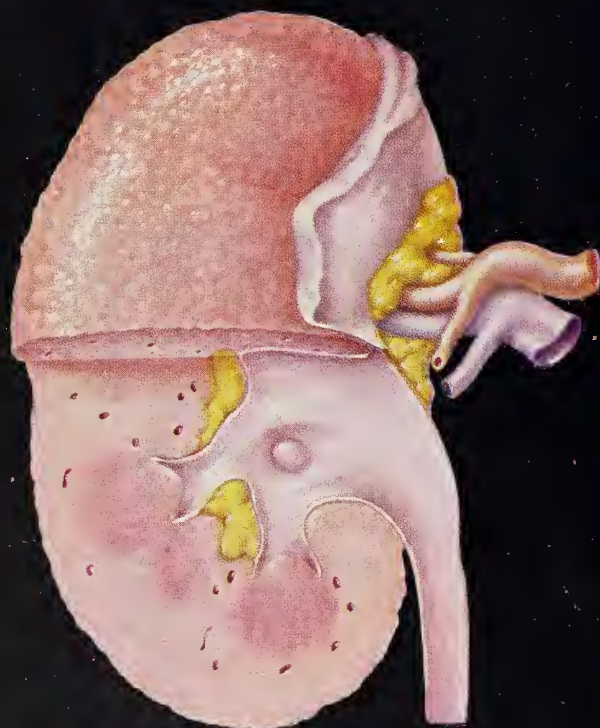
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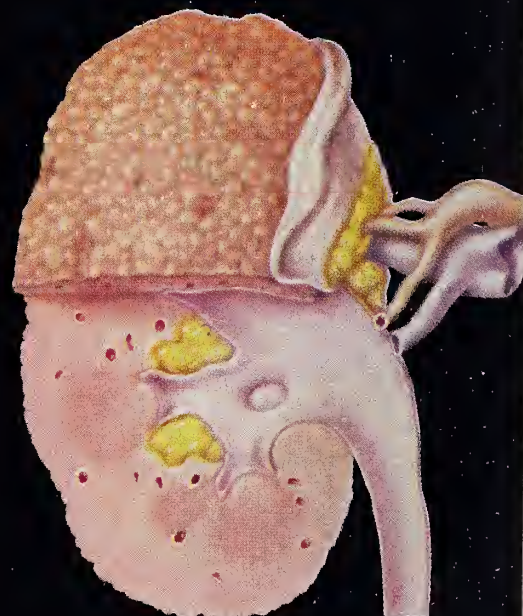
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1. Wolf, R. L., Mendlowitz, M., Naftchi, N. E., and Gitlow, S. E.: Current Treatment of Hypertension with Drugs, Amer. Heart J. 66:414, Sept., 1963.

INDICATIONS: Sustained moderate to severe hypertension.

CONTRAINDICATIONS: Pheochromocytoma and active hepatic disease. Use with caution in history of previous liver disease or dysfunction. Unsuitable in mild or labile hypertension responsive to sedatives or thiazides alone. Not recommended in pregnant patients.

PRECAUTIONS: Observe usual new-drug precautions. Perform hepatic-function tests, white-cell and differential blood counts at intervals during first 6 to 8 weeks or in unexplained fever. If fever occurs without infection, discontinue. Discontinue or reduce dosage in severe reactions. Expect additive antihypertensive effects in combination therapy. Fluorescence in urine samples at same wavelengths as catecholamines may interfere with diagnosis of pheochromocytoma.

SIDE EFFECTS: Sedation often seen during initial therapy or when dosage increased. On initiation, transient headache or weakness may be noted. Occasional orthostatic hypotension, lightheadedness, and symptoms of cerebrovascular insufficiency may occur. Angina pectoris may be aggravated. Bradycardia, nasal stuffiness, mild dryness of mouth, gastrointestinal distress, nausea, vomiting, constipation, diarrhea, weight gain, and edema reported. Rare reactions include: impotence, breast enlargement, lactation, skin rash, sore tongue, mild arthralgia, myalgia, parkinsonism, psychic disturbances including nightmares, reversible mild depression or psychoses, rise in BUN, single case of Bell's palsy, reversible reduction in leukocyte count, reversible agranulocytosis, acquired hemolytic anemia, fever, eosinophilia, mild reversible jaundice, and microscopic focal hepatic necrosis compatible with drug hypersensitivity. Some patients on continued therapy develop a positive direct Coombs' test without evidence of hemolysis, anemia, or related clinical side effects. After exposure to air, urine may darken owing to breakdown of methyldopa or its metabolites.

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## Reports of Physicians Working for Auto Safety

After safety belts have been fastened, dashboards padded, and highways improved, it is still the man or woman behind the wheel who causes or avoids an auto accident.

That's why the driver's doctor hopes he will follow some lifesaving medical advice.

The American Medical Association and many individual physicians are increasing their efforts at accident prevention. More needs to be done, says an AMA publication, if physicians are to have a substantial part in reducing the highway death toll.

One physician, Dr. Lee W. Bass, of Pittsburgh, Pa., personally undertook research with fellow pediatricians to determine the doctor's influence on his patient's safety habits. The doctors counseled 1,423 families in one year.

They found that 43 per cent of the families installed seat belts after receiving face-to-face advice and two letters from the pediatrician. In families which received only the two letters, 15 per cent purchased seat belts.

Dr. Bass concluded: "Personal influence is an effective and powerful tool. When properly applied it can result in rich benefits for the patient and equally rich satisfaction for the physician. It is the duty of all physicians to use this effective tool in the many areas of their practice."

The Essex County (N.J.) Medical Society presented a highly successful public forum in December on "Why You and Your Family Need A Safer Car." The society received cooperation from the community and many groups interested in auto safety. It has prepared suggestions for medical societies planning similar programs.

Research by medical specialists has contributed knowledge about the causes of auto accidents and injuries. In January, Paul W. Gikas, M.D., and Donald Huelke, Ph.D., both on the medical faculty at the University of Michigan, reported their findings involving 136 fatalities in a southeastern Michigan county.

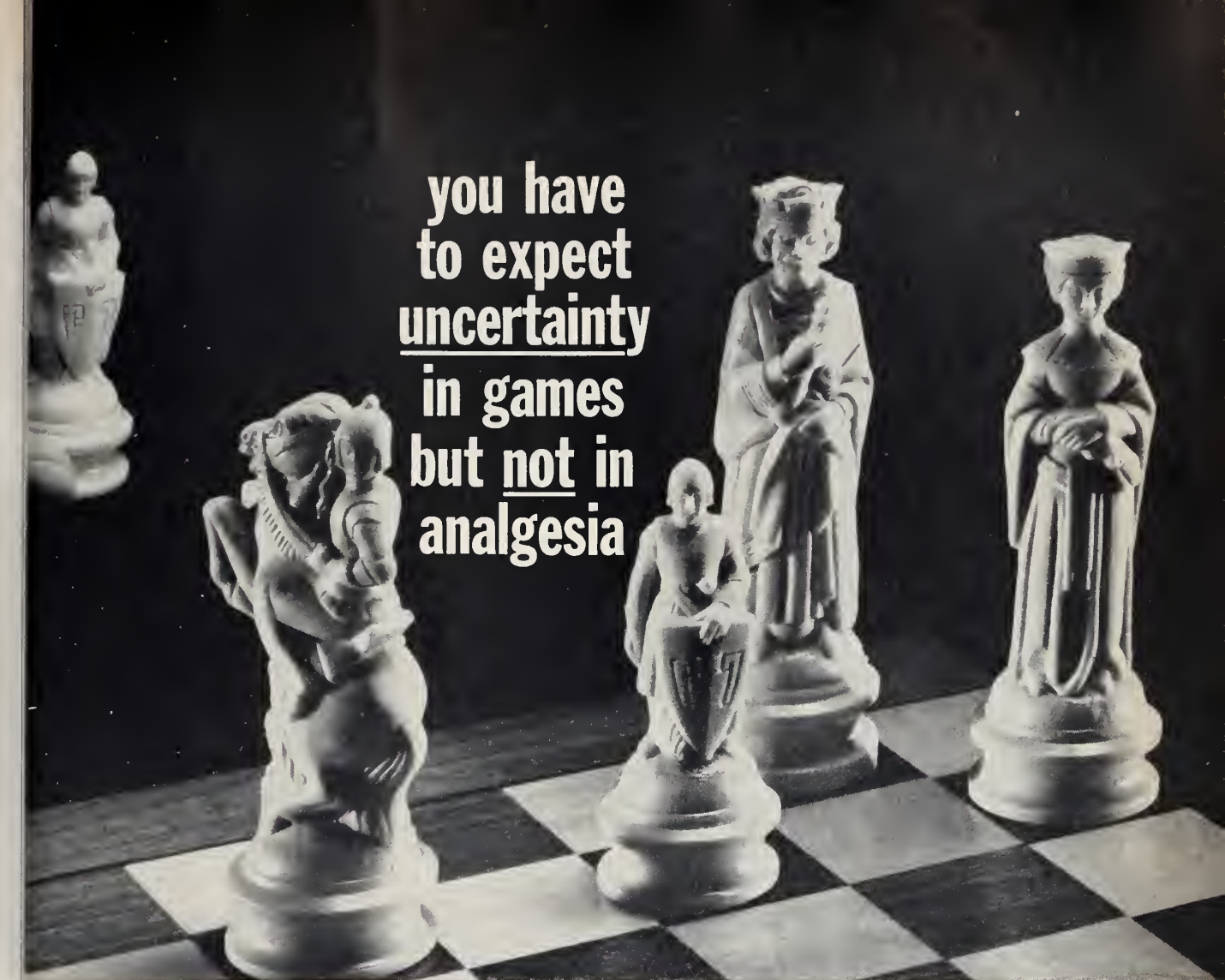
Ejection from the vehicle was the leading cause of death. The majority of these victims could have survived if they had used seat belts, the investigators said. Other than death by ejection, the instrument panel was the foremost cause of death to front-seat passengers, most of whom could have been saved by seat belts.

They concluded that the steering assembly must be improved, dashboard designed in terms of function and safety, and that increased structural rigidity needs to be placed on the car sides, around the doors, the frame, and possibly the roof.

Melvin L. Selzer, M.D., recently reported that

(Continued on Page 32)





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## Population Expansion one of Six Topics of General Sessions at 1966 AMA Annual Convention

Population expansion, a subject much discussed in both medical and lay circles, will be one of six topics presented in general scientific sessions at this year's Annual Convention of the American Medical Association.

The Convention is to be held in Chicago June 26 to 30; the Scientific Program will be at McCormick Place, and the House of Delegates will convene at the Palmer House.

Scientific Sections of the AMA Council on Postgraduate Programs taking part in the General Meeting on population expansion will be Preventive Medicine, General Practice, Internal Medicine, Obstetrics and Gynecology, and Pediatrics. The General Scientific Meetings are open to all physicians attending the Annual Convention.

Other General Scientific Meetings on this year's Annual Convention program will be on the subjects of: emphysema, burns, mysterious fevers, community hospital coronary care units, and headache.

In addition to the General Sessions, each of the 23 Scientific Sections will present scientific programs. Many of the Section programs will, as in past years, be joint meetings of two or more Sections and, in some instances, a specialty society.

Specialty societies joining AMA Sections will include:

—The American College of Chest Physicians, which will join the Section on Diseases of the Chest for an all-day program.

—The American College of Cardiology and the American Heart Association, which will join the Section on Internal Medicine in a half-day session.

—The American College of Clinical Pathologists, which will join the Section on Pathology and Physiology in a half-day session on computers in medicine.

—The International Academy of Pathology, which will join the Section on Pathology and Physiology in a full-day program on tropical medicine.

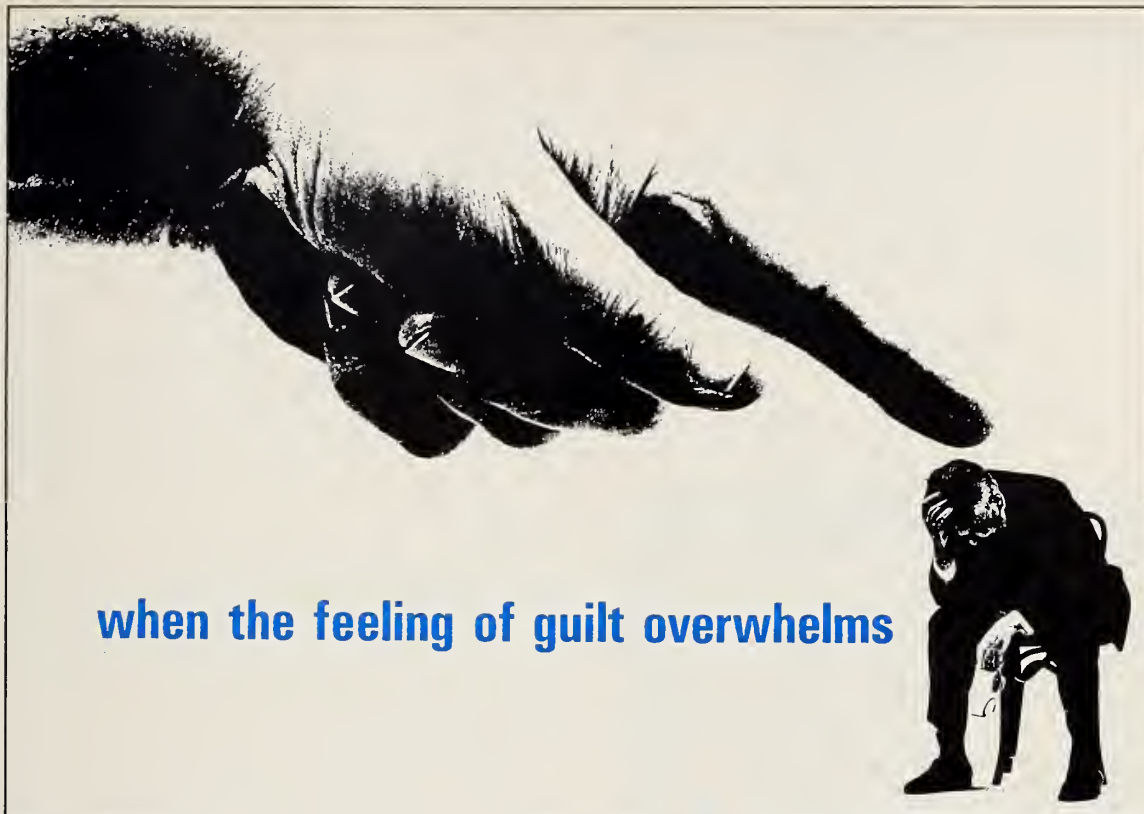
—The Society for Investigative Dermatology, Inc., which will hold its meetings in conjunction with the Section on Dermatology.

—The Association for Research in Ophthalmology, Inc., which will meet in conjunction with the Section on Ophthalmology.

The AMA Committee on Blood and the Section of General Practice also will present a joint half-day program.

The scientific program will open at 9 a.m. Monday, June 27, in McCormick Place. General registration will be in the lower lobby of McCormick Place. It will be open 10 a.m. Sunday, and from 8:30 a.m. to 5 p.m. on following days.





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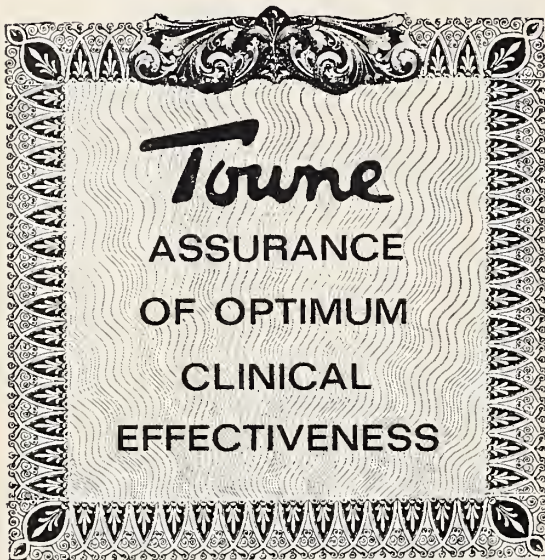
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## Reports of Physicians Working for Auto Safety

(Continued from Page 20)

more than half of the 72 drivers involved in fatal accidents in a 26-month period in his home county of Washtenaw, Michigan, suffered some form of mental illness.

An immediate "short range" accident-prevention program is needed within the medical profession, says Paul V. Joliet, M.D., chief of the U.S. Public Health Service's Division of Accident Prevention.

1. The public must be informed that certain medical disabilities can limit safe driving. If the disability progresses beyond a point, driving must be restricted. If the disability progresses still further, driving under any circumstances becomes impossible.

2. Responsibility to drive safely rests primarily with the individual. Drivers must be taught that the individual is always primarily responsible for any personal actions that endanger the public.

3. Medical advisory committees must be established in each state to provide consultation to motor vehicle administrators about medical fitness of specific drivers.

Physicians are particularly equipped to promote legislation involving medical aspects of traffic safety. Their help is needed in promoting uniform vehicle codes recommended by the National Safety Council, the AMA, and other national organizations.

The AMA Woman's Auxiliary has already urged its members to participate in or sponsor locally the National Safety Council's Driver Improvement Program. The program provides two-hour weekly courses for a month to instruct licensed drivers in the prevention of accidents through "defensive driving."

Medical initiative is needed to promote safe driving, said Abraham J. Mirkin, M.D., of Cumberland, Md., chairman of the AMA Committee on Medical Aspects of Automotive Safety.

"Motor vehicle accidents will be substantially reduced through carefully controlled experimental and clinical studies, epidemiological surveys, and statistical analyses, with the physician working in close collaboration with other biological scientists and engineers," he said.

A past chairman of the committee, Fletcher D. Woodward, M.D., of Charlottesville, Va., said: "It is the physician's duty to inform the public and its legislative representatives of the seriousness of automotive injuries. The physician is proud of his definitive care of the injured, but his duty as a citizen and a physician will not have been fully discharged until preventive measures have become facts and are reflected in the daily accident statistics."



# Eosinophils and Eosinophilia

DONALD L. DONOHUGH, M.D., M.P.H., *Orange*

■ *In their practice of medicine, clinicians occasionally encounter patients with eosinophilia in which the common causes have been satisfactorily ruled out. It is the purpose of this review to present some of the salient features of our present knowledge concerning the eosinophil and to suggest a method for studying eosinophilias of obscure cause.*

EOSINOPHILS ARE FORMED exclusively in the bone marrow<sup>3</sup> and can first be differentiated when the dark metachromatic granules in the cytoplasm of the promyelocyte begin to be replaced by granules with an intense affinity for the acid dye *eosin*.<sup>16</sup> These granules are large, spherical and uniform, and are sufficiently specific to identify the eosinophilic myelocyte in unstained preparations either by ordinary or phase contrast microscopy. A mature eosinophil develops from its myeloblast precursor in approximately 24 hours, as determined by marrow culture techniques.<sup>35</sup> It resembles the neutrophil morphologically in all respects except for the specific granules and in that its nucleus is somewhat larger and is nearly always bilobed rather than multi-lobulated.

## Location

Once formed, mature eosinophils remain in the marrow an average of three or four days and constitute approximately three-fourths of the eosinophilic elements found there.<sup>1</sup> The marrow is the only important reserve of eosinophils in the

body. From the blood stream, perhaps half leave the blood to enter the tissue during the first circulation through the body and most enter the tissue within an hour.<sup>36</sup> It is important to understand that the eosinophil is a cell that has its primary function in the tissue and utilizes the blood stream only for transport.<sup>42</sup> Fewer than 1 per cent of the total number of eosinophils in the body are to be found in the blood.<sup>36</sup> In normal persons, eosinophils preferentially reside in the tissues of the skin, the lung and the gastrointestinal tract.<sup>7</sup> Eosinophils leave these and other tissues by way of the lymphatic channels and those that are injured or senescent are selectively destroyed by the reticuloendothelial system.<sup>1</sup> Their total life span once they leave the marrow is eight to twelve days.<sup>36</sup>

## Composition

Cytochemical study of the nucleus, mitochondria and cytoplasm of eosinophils has shown that they contain the same or similar substances as the neutrophil.<sup>1</sup> The specific granules consist of a phospholipid with a central arginine-rich protein core.<sup>44</sup> Considerably more work needs to be done in the cytochemistry of these granules.

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Electron microscopy has demonstrated that the granules contain a crystalloid formation<sup>3</sup> and microradiography shows the granules to be decidedly radiopaque.<sup>24</sup> Charcot-Leyden crystals are formed by the coalescence of the central electron-dense portion of the eosinophilic granules on disruption of the eosinophil.<sup>45</sup>

## Function

The function of the eosinophil is not yet known with certainty, and one can only form conjectures from the large quantity of experimental material available. They have been shown to respond by margination, diapedesis and migration to the site of the injection of many substances.\* The first injection of a suitable substance results in low-grade tissue eosinophilia, but repeated injections at intervals of three days to one week cause an arithmetic increase of both blood and tissue eosinophilia.<sup>29</sup> Hudson<sup>25</sup> pointed out the importance of considering the increased marrow reserve following the first injection in the evaluation of the eosinophilic response obtained on subsequent injections.

Speirs<sup>41</sup> found that repeated injection of the same or similar substances resulted in a greater eosinophilia than if widely differing substances were used. This implies a recognition on the part of the eosinopoietic system of a previously encountered eosinophilogenic substance. This and the quantitative correlation between antibody levels and eosinophil production, both in their production on exposure to an antigen and in their inhibition by irradiation and steroid therapy, led him to postulate a role for the eosinophil in antibody production. However, the temporal discordance in the appearance of antibody and eosinophils in his and others' experiments, and his failure to consider the magnitude of the marrow reserve in his measurements, have cast doubt upon his conclusions.

Aschkenasy<sup>4</sup> observed that eosinophils respond to the antigen and to the antigen-antibody complex but not to the host's own antibody. Litt<sup>30</sup> concluded on the basis of his experiments that eosinophilia was not involved in the development of antibody but that it was a response to the union of antigen and antibody. Using immunofluorescent techniques, he also demonstrated phagocytosis of

antigen-antibody complexes by eosinophils, confirming Sabesin's finding with electron microscopy.<sup>31</sup> As to the nature of the substances possessing eosinophilotactic and eosinophilogenic capacity, all observers are in accord that they are either proteins or complex polysaccharides or combinations thereof. Constituents such as polypeptides, peptones, amino acids, carbohydrate polymers and monosaccharides have no such effect, nor do lipids.<sup>7,11,12,29,41</sup>

That the host proteins and polysaccharides do not cause eosinophilia is obvious and has been confirmed by autografts, injections of homologous serum proteins and autohemotherapy.<sup>7</sup> Speirs<sup>41</sup> prepared splenic extracts of mice and injected them into genetically identical mice without causing eosinophilia, whereas such preparations when injected into genetically different animals invariably did. It can therefore be concluded that the substances with eosinophilotactic and eosinophilogenic properties are proteins, complex polysaccharides or combinations thereof that are foreign to the host.

The stimulation of eosinopoiesis in the marrow and the release of eosinophils are mediated humorally, as Zaiman demonstrated with parabiotic rats.<sup>49</sup> Archer<sup>2</sup> expressed belief that the humoral substance is histamine, and other investigators<sup>22,44,49</sup> have reported anti-histaminic activity by the eosinophils and phagocytosis by eosinophils of mast cell granules<sup>46</sup> which are the main source of histamine in the body. However, some investigators have suppressed histamine release and anaphylactic symptoms by administering antihistaminic drugs before the injection of an antigen without affecting the eosinophilic response.<sup>40</sup>

In view of the foregoing, what is known of the function of the eosinophil can be summarized as follows. Its preferential location in the epithelial barriers implies a role in the defense of the host and its selective response to foreign protein-polysaccharide compounds further implies that this defensive role is the neutralization of these substances. This defensive role roughly parallels the production of antibody but is linked with it only insofar as both the antigen and antigen-antibody complexes constitute foreign proteins which themselves are eosinophilogenic. Eosinopoiesis, release from the marrow and eosinophilotaxis are medi-

\*Reference Nos. 2, 7, 24, 43, 44, 45.



ated humorally, but histamine does not appear to be the only substance involved.

### Physiologic Variation

The accepted normal blood eosinophil level in humans is from 50 to 250 per cu mm, and although no precise quantitative studies in tissues have been done, more than three or four per high-powered field would be regarded as unusual.<sup>1</sup> Newborns have a blood level averaging 500 to 600 per cu mm<sup>1,4</sup> which decreases to the accepted upper limit of normal within a few weeks of birth and remains within normal limits after the age of one year. This effect has been attributed to a relative adrenal insufficiency at birth. There is a slight fall in old age to the lower limits of normal, according to Buret,<sup>14</sup> possibly due to declining function of the eosinopoietic system. Levels in men tend to be somewhat lower than in women during adult life, and women undergo variation during their menstrual cycle, with a drop at the time of ovulation. Most observers agree on a diurnal variation in both sexes, with the levels being somewhat higher in the morning and lower later in the day. These changes are possibly linked with adrenocortical activity. Depending on their size and content, meals can cause a slight biphasic variation in the blood level also. This has been confirmed by animal study wherein eosinophils were absent from the intestinal wall in the starvation state but there was an intense infiltration when the animal was placed on a high-protein diet.<sup>43</sup>

### Pathologic Variation

Eosinopenia results from exposure to cold, physical exertion, psychic trauma and physical injury. The mediating factor in these conditions is believed to be increased activity of the anterior pituitary-adrenal axis. Epinephrine and histamine when injected also cause eosinopenia and it is generally conceded that this is by stimulating pituitary production of ACTH. The Thorn test of adrenal capacity is based upon this principle.

The exact mode of action of the adrenal steroids in producing blood eosinopenia is not known. There is no lytic effect *in vitro* nor can increased destruction or phagocytosis be demonstrated *in vivo*. It has been rather widely held that their action is one of blocking release from the marrow; but if this were their only effect, eosino-

philic elements in the marrow would increase in proportion to the other elements during steroid therapy. No change is observed either in the number of eosinophilic elements or their mitotic activity in the marrow on initiating or maintaining corticosteroid or ACTH therapy. However, an increase in eosinophilic elements is often noted on cessation of therapy, reflected peripherally by a transient blood eosinophilia. This would suggest a suppressive effect on eosinopoiesis. However, if this were the only effect, a decreased mitosis and steady diminution in the marrow reserve of mature eosinophils should be observed during therapy, and they are not. It would appear from the above that steroids most probably neutralize the humoral substance that stimulates and coordinates both the production and the release of eosinophils from the marrow, but increased generalized dispersion in the tissues as an additional mode of action has not been ruled out.

Eosinophilia is defined by Wintrobe<sup>48</sup> as "the term applied to an increase in the number of eosinophilic leukocytes above the normal (250 per cu mm)," but it must be borne in mind that tissue eosinophilia is the basic phenomenon. On injection of an eosinophilogenic substance, migration of eosinophils from the blood stream to the site of injection begins almost at once. The tissue eosinophilia reaches a maximum in 12 to 24 hours and continues until the substance is neutralized. In the meantime, blood eosinopenia can be noted within an hour and the nadir is reached in two to four hours. In the marrow, a depletion of the mobile reserve can be detected four to six hours after the injection, and an increase in eosinopoiesis in approximately 12 hours. This results in blood eosinophilia in about 24 hours that continues until the injected substance is neutralized.<sup>20</sup> Thus the blood level may be low, normal or high with a true tissue eosinophilia, and even continue high after the tissue reaction has ceased.

The factors causing eosinophilia in the laboratory have been mentioned, and now the causes of eosinophilia from the clinical standpoint will be considered. The terms *mild* (to 10 per cent), *moderate* (10 to 30 per cent) and *marked* (over 30 per cent) will be used to give an approximate idea of the blood levels, and *transient* (a month or less) and *persistent* (more than a month) will be used to give some idea of their duration.

1. Eosinophilic leukemia has been reported to produce marked and persistent eosinophilia. Bent-

ley and coworkers<sup>6</sup> presented a comprehensive review of the literature on this problem. Using the definition of "a marked eosinophilia in the peripheral blood with blast cells above normal in the bone marrow and/or the peripheral blood," they were able to accept 20 cases from the literature but had to discard some 37 other reports of "eosinophilic leukemia." If one uses the definition of Bousser<sup>9</sup> that the case must be similar to myeloid leukemia throughout its course, but have immature eosinophils as a constant and predominant feature in the peripheral blood, then the number of acceptable cases in the literature is reduced to approximately 15. If one insists further on the demonstration of eosinophilic myeloblasts and promyelocytes in the marrow, the number is reduced to zero. Thus the disease is a strangely rare one by any acceptable definition. A pattern perhaps emerges when one notes that some of the reported cases are clearly myelogenous leukemia with a superimposed eosinophilia consisting entirely of mature eosinophils. This might represent an eosinophilic response to some abnormal proteins produced in the leukemic process or be a non-specific reflection of the abnormal marrow activity. Most of the other cases appear to be myelogenous leukemia also, but in these a variable number of immature eosinophils is found in the peripheral blood. This suggests a spectrum in myelogenous leukemia in which the eosinophil precursors may be either uninvolved, partially involved or totally involved. If this is so, then it might be better not to classify eosinophilic leukemia as a separate entity but to consider these cases as myelogenous leukemia and append a description of the extent to which the eosinophilic elements are involved.

2. Periarteritis nodosa is not ordinarily accompanied by eosinophilia, but it has been reported in up to 30 per cent of the cases in which pulmonary symptoms and pathologic changes were present. It is usually a mild, persistent eosinophilia but marked eosinophilias have been described. Some of the reported cases have not had the typical lesions but rather a form of endarteritic thickening with focal necrosis and thrombus formation. These may represent the vascular counterpart of Löffler's endocarditis parietalis fibroplastica with eosinophilia.<sup>47</sup> It is interesting to note that in several of the cases which could not be accepted by Bentley and coworkers as eosinophilic leukemia, the patients died in con-

gestive heart failure after a prolonged course, and at necropsy there was myocardial infiltration by eosinophils and fibrosis with mural thrombi.<sup>19</sup> In all of these entities a common denominator of a blood-borne antigen causing the vascular reaction is suggested,<sup>23</sup> and morphologic equivalents have been described<sup>8</sup> that would lend support to their consideration as a group until the precise etiologic factors involved are elucidated.

3. Allergic disorders such as allergic rhinitis, asthma, angioneurotic edema, urticaria and serum sickness regularly manifest eosinophilia. This may be quite marked in the involved tissue and the cellular exudate but the blood eosinophilia is almost invariably mild. The duration of the eosinophilia corresponds to the patient's exposure to the antigen.

4. Medications, especially when given parenterally, can cause eosinophilia. The list of those reported is almost endless. This appears to be due to a constitutional characteristic of certain individuals wherein the medication is able to combine with and alter a host protein to form an antigen.<sup>15</sup> The eosinophilia is usually moderate but may be marked, and is transient.

5. Destructive dermatoses such as eczema, dermatitis herpetiformis, pemphigus and psoriasis can cause an eosinophilia that varies with the duration and extent of skin involvement. Any destructive lesion of an epithelial surface, such as those found in certain types of pneumonia and ulcerative colitis, for example, are capable of causing eosinophilia also, and the mechanism is believed to be the alteration of host protein in these sensitive areas. Tumors of epithelial surfaces (gastrointestinal tract, lung, skin, cervix and elsewhere) can cause a persistent, and mild to moderate eosinophilia. A neoplasm with origin elsewhere but metastasizing to a serosal surface occasionally has the same effect. Eosinophilia tends to be more frequent with tumors undergoing central necrosis.

6. Convalescence from a febrile illness often results in a mild and transient eosinophilia due to the cessation of adrenal hyperfunction and perhaps also to the production of antigen-antibody complexes.

7. Radiotherapy in repeated doses can cause a mild or moderate transient eosinophilia, apparently by altering host tissue.

8. Splenectomy can result in a mild but persistent eosinophilia starting as late as a year



after operation. The reason is not clear, but perhaps has to do with removal of the main organ of eosinophil destruction.

9. Hodgkin's disease is accompanied by eosinophilia in 5 to 10 per cent of the cases (up to 20 per cent in some series). It is most often mild and persistent, but may be marked.<sup>33</sup> It is more frequently found in abdominal Hodgkin's disease where ulceration of Peyer's patches has been demonstrated and thus it might possibly be due to the decreased integrity of the intestinal epithelial barriers in excluding intestinal contents. Production of an abnormal protein is another possible explanation.

10. Löffler's syndrome has stood the test of time as a workable clinical classification, but in using the term one must be careful to heed the original definition.<sup>32</sup> The eosinophilia is mild and transient. Crofton,<sup>13</sup> created a classification of pulmonary diseases accompanied by eosinophilia that has proven useful in cases that do not fit Löffler's definition, although the categories are grouped according to severity, which is not necessarily concordant with etiologic factors.

Approximately 50 per cent of patients with Löffler's syndrome have a history of allergic diathesis in themselves, in collateral relatives, antecedents or progeny, and it is now the consensus that the syndrome is produced by the pulmonary migration of intestinal parasites (especially *Ascaris*) in presensitized or predisposed persons.<sup>13</sup>

11. Tropical eosinophilia<sup>17</sup> and the Meyers-Kouwenaar syndrome<sup>34</sup> are believed to be caused by zoonotic filarids.<sup>10</sup> In both, the eosinophilia is marked and persistent.

12. Cutaneous larva migrans results from skin contact with soil containing larvae of certain zoonotic parasites.<sup>21</sup> The eosinophilia tends to be very mild but persistent.

13. Visceral larva migrans is caused by migration throughout the human body by larvae of zoonotic helminths.<sup>5,38</sup> In this category should be included gnathostomiasis, sparganosis and the eosinophilic meningoencephalitis first reported in Tahiti.<sup>45</sup> Eosinophilia tends to be moderate to marked and persistent. It is now believed that the entity "familial eosinophilia" is actually visceral larva migrans, with several members of a family being infected from a common environmental source.

14. Parasites for which the human is accepted

as an intermediate or definitive host cause the majority of the cases of mild eosinophilia encountered clinically.<sup>26</sup> The degree varies with the nature of the parasite, its location or migration in the host, and the intensity of the infection. The duration varies with the exposure to the parasite and its products. Protozoa, like viruses, bacteria and fungi, do not cause eosinophilia except secondarily through epithelial destruction.

In the metazoa, the mature cestode in the gut does not usually cause eosinophilia, but if great numbers are attached to the mucosa as with *Hymenolepis nana*, there may be mild eosinophilia. When man is the intermediate host as in echinococcosis and cysticercosis, oncospheric migration and cyst rupture with extravasation of its contents can cause a moderate to marked but transient eosinophilia.

Among the trematodes, those which reside in the intestinal lumen do not usually cause eosinophilia; those in the biliary tract usually cause a mild, persistent eosinophilia which may become moderate during migration and oviposition; those inhabiting the veins of the intestine and bladder cause a persistent mild to moderate eosinophilia which may be marked during metacercarial migration and oviposition. *Paragonimus westermani*, which resides in the lungs, causes a mild to moderate eosinophilia varying with the intensity of the infection.<sup>18</sup>

In nematodes, those living free in the intestinal lumen or superficially attached to the mucosa do not cause eosinophilia. However during migration of the larvae through the lungs, a moderate to marked but transient eosinophilia results. Those which invade, live in and deposit larvae in the intestinal wall and other tissue cause a moderate to marked eosinophilia. Filarids cause a variable eosinophilia depending upon the characteristics of the species. *Dracunculus medinensis* is usually sheathed in a fibrous capsule and rarely causes eosinophilia. The adults of *Onchocerca volvulus* also tend to remain in fibrous onchocercomas but discharge microfilariae, and may therefore cause a persistent eosinophilia of mild proportions. The adult *Loa loa* migrates in the subcutaneous tissues and also produces microfilariae; thus the resulting eosinophilia is usually moderate. Among the arthropod ectoparasites, only *Sarcoptes scabiei* and *Tunga penetrans* invade the skin to any extent, and with them eosino-

philia is rare and mild when it does occur. Myiasis caused by the larvae of many cyclorrhaphous flies is rarely accompanied by eosinophilia, as their migration is minimal and the larvae tend to become enclosed in fibrous capsules.

## Diagnosis

A systematic approach is required in the diagnosis of eosinophilias, because the usual investigation may fail to lead to a diagnosis in as many as 60 per cent of the cases, and the patients therefore do not receive specific treatment.<sup>27</sup> The first step is to obtain one or more absolute eosinophil counts to make sure that eosinophilia actually exists, to ascertain the level of eosinophilia and to establish a baseline against which to measure the progress of the disease and the effect of therapy. As eosinophils tend to adhere to the glass edge and congregate at the tail of the smear, a report based on the percentage encountered in the smear is subject to laboratory error of up to 20 per cent.<sup>43</sup> Evaluation should then proceed as follows:

1. A complete history must be taken, with emphasis upon allergic diathesis; geographic areas visited during the past year; contact with animals and their excreta; geophagia or pica; eating meat, fish, shell fish or aquatic plants raw or poorly cooked; skin contact with the ground and with fresh water streams or lakes; medications taken within past month; and recent febrile illnesses, radiation or splenectomy. In the system review particular attention should be paid to the skin and the gastrointestinal and respiratory tracts.

2. The physical examination must include a careful examination of the skin with scrapings of wheals or other lesions for eosinophils; palpation for nodes and hepatic or splenic enlargement; examination of the nasal mucous membranes with a smear for eosinophils if the membranes appear to be involved; careful examination of the chest and abdomen for evidence of respiratory or gastrointestinal disease; and a rectal-sigmoidoscopic examination. Women should have a pelvic examination with a Papanicolaou smear.

3. Absolute eosinophil counts of the peripheral blood should be done periodically, and blood smears should be examined at the same time for blood-borne parasites and immature eosinophils. If immature cells are found, a bone marrow aspiration is indicated.

4. If respiratory symptoms are present, at least three specimens of sputum should be examined for malignant cells, ova, parasites, eosinophils and Charcot-Leyden crystals. Bronchoscopy with aspiration and other specialized procedures can be considered.

5. An x-ray film of the chest, an upper gastrointestinal series and studies with barium enema should be routine in all cases.

6. At least three fresh stools should be examined by a competent experienced laboratory technician for ova and parasites, and at least one specimen should be studied with a concentration technique. If strongyloidiasis is suspected, duodenal intubation and aspiration should be considered. If schistosomiasis is a possibility, the urine sediment must be examined carefully. The stools should be routinely examined also for occult blood, eosinophils and Charcot-Leyden crystals.

7. A panel of liver function tests is indicated.

8. Biopsy of any suspicious skin lesion is required. If such lesion is present, then biopsy of a specimen of the skin, including subcutaneous tissue and muscle, taken at random should be done.

9. Biopsy of one or more specimens of the liver is indicated if there is hepatomegaly, liver tenderness or alteration of the liver function tests. Specimens must be divided into three portions and examined as fresh press preparations, after pepsin digestion, and as serial sections of fixed tissue.

10. Biopsy of enlarged or tender nodes must be done, using the same examination techniques as for the liver.

11. Skin tests using parasite antigens are of value only if negative, due to the persistence of positivity and the frequency of cross reactions. Serologic methods of value in some parasitic diseases have been developed and serum can be sent to health centers and institutions that perform these tests. Increasing reliability and specificity is being obtained by investigators active in this field.<sup>28,37</sup>

By following the rules set forth above, the author has been able to make specific diagnosis in most cases. However, if the eosinophilia remains etiologically obscure despite this investigation, continued observation during careful therapeutic trials is the only remaining resource.

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# Pulmonary Alveolar Proteinosis

## Review of the Literature with Follow-up Studies and Report of Two New Cases

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■ *In the period from 1958, when Rosen and coworkers first reported a condition in which the pulmonary alveoli are filled with an eosinophilic material, to the beginning of 1964, reports of 93 cases had accumulated in the world literature, including two cases included herein. The cause of this disease, which Rosen called "pulmonary alveolar proteinosis," is not known, nor is there a known means of cure.*

*The usual patient is a white man between 30 and 50 years of age who may do any kind of work. The first symptoms may be those of pulmonary infection or pulmonary insufficiency. Patients with pulmonary alveolar proteinosis are prone to nocardiosis and infection with other fungi. Diagnosis is made by lung biopsy.*

*Twenty of the 93 patients reported upon were alive at the time of this review, 37 were dead and 36 had been lost to follow-up.*

IN 1953, Linell and coworkers<sup>56</sup> reported a 57-year-old joiner who had begun to have easy fatigability and a mild, slightly productive cough six years before his death. At the onset of these symptoms, x-ray films of the chest showed densities in both lower lung fields, and these abnormalities persisted through the years. About a year before he died, facial pustules developed and *Cryptococcus neoformans* grew on cultures of material from them. This organism was also cultured from the spinal fluid, the blood and material washed from the stomach. At autopsy destruction of the right lower lobe of the lung by masses of cryptococci was observed. On examination of the pneumonia-like foci in the left lung, unusual microscopic features were noted which were not epithetically described until Rosen in 1958 used the term *pulmonary alveolar proteinosis*.

Submitted 30 September 1965.

As chief of the Pulmonary, Mediastinal and Ear, Nose and Throat Pathology Section of the Armed Forces Institute of Pathology, Rosen had received from puzzled pathologists throughout the country 16 different biopsy specimens of lung tissue in which these characteristics were present. Then Castleman at Harvard Medical School reported four similar cases and Liebow of Yale added seven, making a total of 27 patients in whom the particular pathological features termed pulmonary alveolar proteinosis were reported to have been observed.

To the question, "Could this disease have been overlooked by pathologists until recently?", pathologists answer that the microscopic features are too distinctive to have been missed. Use of hematoxylin and eosin stains shows a granular and floccular acidophilic material filling large groups of alveoli. Small acicular spaces are scattered



throughout this acidophilic substance. This acidophilic substance, referred to as "proteinaceous" material, is periodic acid-Schiff positive.

This alveoli-filling material may originate from the large mononuclear cells in the walls of alveoli, the so-called "septal cells," which slough into the alveoli and undergo necrosis.<sup>90</sup> If this is so, the material may be related to the neonatal pulmonary hyaline membrane, as Barter and Maddison<sup>5</sup> believe that this membrane originates from necrosis of epithelial cells in the respiratory bronchioles. Other investigators think that this alveolar-filling material is a transudate.

## Etiology

Taxay and coworkers,<sup>104</sup> reporting a case of pulmonary alveolar microlithiasis and pulmonary alveolar proteinosis, said:

"We believe that although alveolar proteinosis, pulmonary corpora amylacea and pulmonary alveolar microlithiasis may be different diseases, the evidence to substantiate their separation is far from conclusive. We suggest that pulmonary alveolar microlithiasis and pulmonary alveolar proteinosis represent inherent defects of the pulmonary alveolar capillaries, so that in response to normally encountered inhalants a flux of plasma ultra-filtrate occurs and, following contact with ambient air, resorption becomes impossible owing to physicochemical change . . . [and] calcification may occur."

In the rather complicated case reported by Williams and coworkers<sup>106</sup> calcification of pulmonary alveolar contents had occurred. "The alveolar walls," they said, "showed moderate patchy fibrosis, which in general contained no inflammatory cells. In a few areas the alveolar contents had calcified *in toto*, apparently having shrunk to form a group of calcified, often laminated bodies embedded in dense fibrous tissue."

The chest x-ray film of a patient with pulmonary alveolar proteinosis frequently resembles that seen in acute pulmonary edema. However, comparisons of the pathologic features of these diseases indicate that they are separate entities. Mendenhall and coworkers,<sup>68</sup> after reviewing 532 cases of pulmonary edema, concluded that pulmonary edema was not related to pulmonary alveolar proteinosis.

There is another peculiar lung disease called pneumocystis carinii pneumonia, or interstitial

plasma-cell pneumonia, which resembles pulmonary alveolar proteinosis radiographically and pathologically. In the pneumocystis infection the alveolar contents are said to be reticular and foamy. While only a few cases of pneumocystis pneumonia have been reported in this country,\* it is said to be quite common in Europe. The cause of this lethal pneumonia is thought to be a small, round organism which stains positively with silver chromate and is confined to the alveolar spaces. Since this "organism" has not been cultured nor the disease transmitted to laboratory animals, its relationship to the disease is not clear.

The difficulty of distinction is illustrated by noting that Dick and coworkers,<sup>26</sup> in 1957, reported on two patients with "pneumocystis carinii infection" who later were reported by Rosen<sup>90</sup> as cases 19 and 20 in his collected series of 27 patients with pulmonary alveolar proteinosis. The roentgen findings in pneumocystis carinii pneumonia have been described as a finely granular peripheral pattern distributed throughout both lung fields, not unlike the pattern of peripheral atelectasis seen in hyaline membrane disease.<sup>30</sup> While pneumocystis infection is reported to be a disease of premature infants, a few adults have been reported as having it. Hendry and Patrick<sup>44</sup> reported 13 cases of pneumocystis carinii pneumonia occurring in patients seriously ill with other diseases such as leukemia and lymphoma.

## Reports of Two Cases

**CASE 1.** A 52-year-old white man, a printer, first noted onset of shortage of breath in July 1961. It rapidly increased in severity and within three months the patient had dyspnea, with coughing, on slight exertion. His main complaint was, "I have to pant to breathe." He had been raising small hard "chunks" of sputum. Until the present, the patient had always been healthy. He had lived in Tampa, Florida, until moving to Sacramento in 1947. He had been a printer all his adult life and had had no known exposure to toxic fumes or dust.

On physical examination the patient appeared to be healthy and well developed. He was slightly obese. The only abnormalities noted were dullness and diminished breath sounds over both lower lung fields. Rales were not prominent.

Routine small chest x-ray films on 14 October

\*Reference Nos. 14, 30, 44, 50, 91.

1960 and 27 June 1961 had been reported to be normal. A 14 × 17-inch film on 11 September 1961 showed extensive bilateral infiltration, giving the lungs an opaque, hazy, slightly granular appearance (Figure 1).

No striking changes were observed on bronchoscopic examination but bronchograms showed very little patency of the lower lobes, due to a consolidation process. Cultures of the tracheo-bronchial aspirate were negative for fungi and bacilli.

On 3 October 1961 right thoracotomy was done and biopsy material was taken from the right lower lobe of the lung. Most of the right lung, with the exception of the apex of the right upper lobe, was solid and liver-like to palpation. The visceral pleural surfaces were covered with small yellow plaques. Caseous whitish-yellow exudate oozed from the cut surface of the lung.

### Pathologist's Report

Microscopic examination of the lung showed that the pulmonary alveoli were distended with a slightly broken-up acidophilic debris. The debris for the most part was relatively acellular with only an occasional nucleus contained within and rarely showing globule formations of more intense acidophilia. Rare dissolved-out acicular slits were noted. The alveolar septations are reduced to mere fibrovascular remnants with focal zones exhibiting a delicate infiltration of rounded cells and anthracotic pigmentation. Occasionally seen were masses of xanthomatous type macrophages with numerous multinucleate giant cells usually against a pulmonary trabeculation; small giant cells of six nuclei were occasionally plastered against a septal wall.

Pathological diagnosis: pulmonary alveolar proteinosis.

Postoperatively the patient did well until the third day, when fever to 39.4°C (103°F) developed. Cultures of the sputum revealed no specific pathogen. One suture became infected with staphylococci. The infection cleared rapidly with erythromycin therapy. In spite of active therapy including prednisolone intravenously, potassium iodide and antibiotics (no penicillin or sulfadiazine were given because of a history of allergic sensitivity to these drugs) the condition of the patient continued to worsen and he died 22 October 1961, due to anoxia. At autopsy consolidation of both lungs was noted. The lower lobe of the right lung was extensively destroyed by a suppurative reaction.

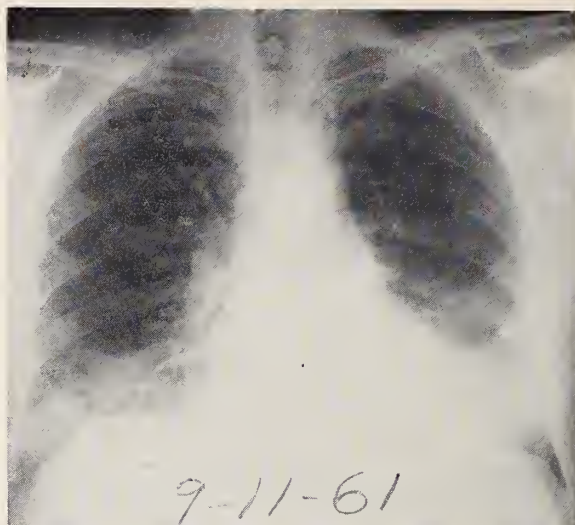


Figure 1.—Chest x-ray of Case 1 showing the characteristic changes in the lungs of patients with pulmonary alveolar proteinosis; the involvement is typically lower lobe and bilateral.

Microscopically extensive pulmonary alveolar proteinosis was noted in both lungs. In some areas microabscesses and macroabscesses were seen. Cultures from the abscess cavities yielded *Nocardia asteroides*.

CASE 2. A 40-year-old white male salesman noted the onset of a dry cough, tightness in the chest, with pain in the left side of the chest and the left shoulder, in June 1963. He sought medical attention in September 1963. At that time he also complained of severe nervousness and admitted excessive intake of alcohol. He was disturbed by marital problems. The patient knew of no known exposure to toxic dusts or fumes except that he was a heavy smoker of cigarettes. He had noticed rasping voice and change in tonal quality over the preceding six months.

Except for those mentioned by the patient, no abnormalities were noted on physical examination. Results of extensive laboratory investigation were all within normal limits. No abnormalities were seen bronchoscopically and cultures of aspirated tracheo-bronchial secretions grew no pathogens. An x-ray film of the chest showed patchy and linear densities in both lungs (Figure 2). Bronchograms were within normal limits.

Left thoracotomy and excision of biopsy material from the lower lobe of the left lung were performed 21 September 1963. On palpation, diffuse nodulation within the substance of both lobes of the left lung was noted.



## Pathologist's Report

Microscopic study of the excised lung tissue showed an acidophilic material ranging from homogeneous to finely granular intermingled with still identifiable red blood cells filling clusters of alveoli and occasionally alveolar ducts and terminal bronchioles.

Pathological diagnosis: pulmonary alveolar proteinosis.

The patient recovered from the operation without difficulty and at last report, 18 months later, still had extensive pulmonary disease as shown by x-ray films of the chest.

## Analysis of Reported Cases

Up to the first of 1964, 93 cases of pulmonary alveolar proteinosis had been reported, including the two cases herein. From correspondence with the authors of all the reports, it was learned that 20 of the patients were known to be alive at the beginning of 1964, 37 dead and 36 lost to follow-up. Seventy-four of the 93 patients were males and 19 females. Seventy-seven were white, 12 were Negroes, three were Japanese and one Chinese. Fifty-eight of the 93 patients were between 30 and 50 years of age. The youngest was two and a half years old, the oldest 72.

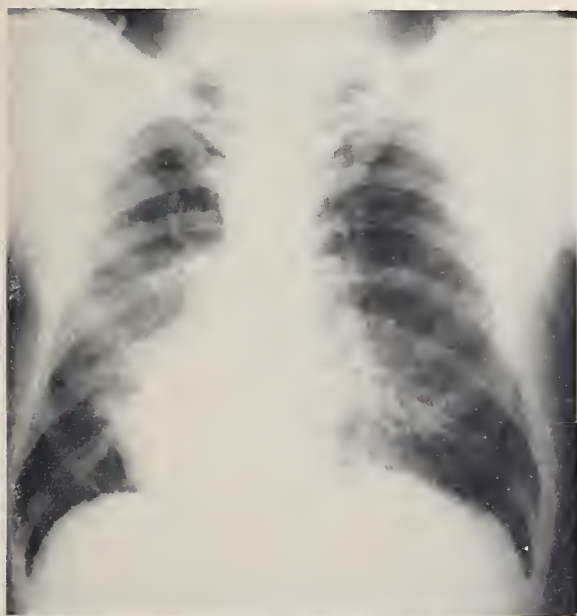


Figure 2.—Chest x-ray of Case 2. Infiltration is present in both lungs but is more pronounced in the left mid-lung field. Diagnosis of pulmonary alveolar proteinosis by left lung biopsy on 21 September 1963. Patient alive and well as of 22 April 1966.

The patients were of a wide variety of occupations, and there was no consistent history of extraordinary exposure to fumes or dusts.

## Symptomatology

Furst and coworkers<sup>38</sup> reported the case of a patient with extensive pulmonary alveolar proteinosis who had no symptoms; evidence of the disease was noted on routine x-ray examination of the chest. It was thought that the disease had probably been present for at least four years but without causing symptoms. Similarly Oka and coworkers<sup>74</sup> reported the case of an asymptomatic 19-year-old girl with extensive disease seen on a routine x-ray film of the chest.

More commonly the symptoms which cause the patient to seek the aid of a physician are those due to pulmonary insufficiency—namely, dyspnea on exertion, cough, fatigue and, less commonly, cyanosis. Frequently a history will be given of recurrent attacks of severe upper respiratory tract infection or pneumonia. The patient may present with chills, fever, cough, blood-flecked sputum and pain in the chest. The more seriously ill patients will have dyspnea at rest, cyanosis, clubbing of digits and hemoptysis. The patient may volunteer that he has been coughing up small “chunks” of material.

## Physical Examination

The patient is usually a well developed, well appearing white man between 30 and 50 years of age who may present few abnormalities. Breath sounds over the lower lung fields may be diminished, with dullness and a few rales present. The more seriously ill patients have dyspnea at rest, cough, cyanosis and clubbing of the terminal phalanges.

## Laboratory Work

Most patients with pulmonary alveolar proteinosis have been extensively investigated. Most important in the investigation are roentgenograms of the chest and cultures of the sputum.

The frequent occurrence of fungus infections and pulmonary alveolar proteinosis indicates the need for searching the tracheo-bronchial aspirate and any other suspected area for organisms. Usually, moderate polycythemia exists, due to the stimulating influence of hypoxia. With infection the leukocyte count rises as expected.

## *Roentgenographic Examination of the Chest*

Features on x-ray films of the chest in pulmonary alveolar proteinosis are more or less characteristic. As seen on roentgenograms, both lower lung fields are involved. Sometimes the lesions have been confused with acute pulmonary edema, which they resemble radiographically. Roentgenologists have variously described the lesions as, "a granular lower lobe infiltrate, bilateral," "a fine, diffuse, perihilar, radiating feathery or vaguely nodular soft density resembling in its butterfly distribution the pattern seen in severe pulmonary edema," and "diffuse linear strands radiating from both hilar areas, bilateral."

On the other hand the lungs may be severely involved and yet appear to be normal roentgenographically.<sup>12,13</sup> This is especially deceiving when on x-ray films the lesion may appear to clear. Burbank and coworkers<sup>13</sup> reported a patient with pulmonary alveolar proteinosis and nocardiosis who was apparently cured of both diseases. The patient died of mesothelioma. Roentgenograms before death showed clear lung fields; also biopsy of a small specimen of the lung revealed no proteinosis, but at autopsy 10 days later extensive pulmonary alveolar proteinosis was found in both lungs.<sup>12</sup>

Repeated x-ray films may show no change for years, or there may appear to be clearing, or it may get worse. So far, complete resolution of the pulmonary disease has not been proved in any case.

## *Diagnosis*

The diagnosis has been established by lung biopsy or at autopsy, with the following exceptions: one patient with a typical history and roentgenographic findings did not have biopsy, but study of "white and chunky" sputum was thought to be indicative of pulmonary alveolar proteinosis; one patient had biopsy of a specimen obtained with a Vim-Silverman needle; two patients reported by Rosen and coworkers did not have lung biopsy but did have roentgenograms typical of the disease.

The possibility of error if the biopsy specimen is too small has already been illustrated in the previously mentioned case reported by Burbank.

It was pointed out by Lundberg<sup>58a</sup> that, due to the presence of mucopolysaccharides in normal and abnormal tissue, colloidal-iron stain of

coughed-up material is not diagnostic for pulmonary alveolar proteinosis.

## *Analysis of Patients Who Have Died*

Of 37 patients with pulmonary alveolar proteinosis who are known to be dead, 19 had complicating diseases and the remaining 18 died of the hypoxic effects of pulmonary alveolar proteinosis. Eight of these patients had superimposed nocardiosis and four had cerebral abscesses. The duration of the disease varied from three months to 17 years.

## *Analysis of Patients Still Alive*

Twenty patients are known to be alive with pulmonary alveolar proteinosis. All of them still have evidence of the disease with the possible exception of one patient who is said to have no pulmonary lesions visible on x-ray films of the chest.<sup>48,88,94</sup> One patient had had the disease for 18 months at the time of this report and the others for over four years. One patient<sup>64,65</sup> has had pulmonary alveolar proteinosis for 17 years. No specific treatment has been found to be effective.

## *Pulmonary Alveolar Proteinosis and Fungus Infection*

Ten patients with pulmonary alveolar proteinosis also had nocardiosis.\* Eight of these patients are dead. One patient<sup>20,21</sup> had a cerebral abscess due to nocardia but is improved. One patient had an abscess due to nocardia of the left flank but is improving.<sup>1,46</sup> One<sup>61,62</sup> had pneumonia due to streptomyces but recovered. In two cases superimposed cryptococcosis was observed at autopsy.<sup>56,90</sup> One patient died with disseminated mucormycosis.<sup>47</sup> One had aspergillus infection of the lung.<sup>27</sup> A draining lesion of the scrotum developed several months before death in one case.<sup>70,92</sup> Two patients<sup>11,83</sup> were reported to have sputum positive for acid-fast bacilli.

## *Nocardiosis*

As nocardia is being cultivated from various infections of patients with pulmonary alveolar proteinosis with increasing frequency as noted above, a consideration of nocardiosis is in order.

Nocardia and actinomyces are mycobacteria and members of the order of actinomycetales. Nocardia asteroides, the causative organism in most

\*Reference Nos. 1, 3, 13, 16, 20, 21, 84, 85, 90, 103.



cases of nocardiosis, is an aerobic, Gram-positive, branching filamentous fungus, variably acid-fast.

Over 213 cases of nocardiosis have been reported.<sup>†</sup>

Nocardiosis may run a rapidly fulminating fatal course or may be prolonged and chronic. Any tissue may be affected but the commonest site of infection is the lung. Next in order are the brain, the skin and subcutaneous tissues, and the pleura. Nocardiosis may simulate many other diseases<sup>42a</sup> or may occur coincident with other diseases.

Raich and coworkers<sup>84</sup> reported nocardiosis occurring with sarcoidosis, pulmonary tuberculosis and cancer of the lung. Stein and Estrellado<sup>101a</sup> reported the fourth case of pulmonary tuberculosis and nocardiosis. Freese and coworkers<sup>36</sup> reported 11 patients with nocardiosis. Nine were cured by sulfonamide therapy and two who had brain abscess, died. Webster<sup>105a</sup> reported 10 cases of pulmonary nocardiosis. Hathaway and coworkers<sup>42a</sup> reported 14 cases, with 11 of the patients recovering. Nocardiosis was superimposed on tuberculosis in two patients, chronic lymphatic leukemia in one and generalized sarcoidosis in one. Cross and coworkers,<sup>23</sup> reviewing 44 cases from the files of the Armed Forces Institute of Pathology, concluded that nocardiosis was primary in 27 cases and that, in the remaining 17, other serious diseases antedated the nocardial infection.

*Nocardia* is not normally found in the human respiratory tract: Raich and coworkers<sup>85</sup> were unable to isolate any nocardia at all from 235 specimens of sputum, gastric washings and tonsils from 109 patients.

Since nocardia are easily cultured and treatment with sulfonamides is usually successful, one must keep the agent in mind particularly when dealing with pulmonary alveolar proteinosis.

For the successful treatment of a very severe case of nocardiosis with all imaginable complications, one should refer to the report by Pellegrin and Henderson.<sup>78</sup> This case was also unusual in that the patient was moribund when massive doses of penicillin saved her life. Sulfonamides were not effective in that case.

## Treatment

Patients with pulmonary alveolar proteinosis have been treated with numerous agents but no specific agent can be said to have been found. Ramirez and coworkers<sup>86</sup> have attracted some at-

tention by the use of "segmental bronchial flooding," in which saline solution heparin or other agents are introduced into certain areas of the lung through a small indwelling catheter which has been passed through the larynx.

Several patients have had trypsin administered in oxygen aerosol by intermittent positive pressure, but most of the patients with pulmonary alveolar proteinosis who are still alive have had no special therapy.

The patient who has had pulmonary alveolar proteinosis for the longest time, 17 years, is a Chinese who is now 69 years old. This patient was reported by McDowell and coworkers<sup>65</sup> as having had "pneumonia" in 1947 and subsequently required numerous periods in hospital. In November 1952 he was again put in hospital with progressive dyspnea, cyanosis and almost complete opacification of both lungs on x-ray films of the chest. A lung biopsy in 1953 established the diagnosis of pulmonary alveolar proteinosis. After this the patient improved and has remained well. As of December 1963 the patient was reported by McDowell to be working hard in his green-grocery business. McDowell believed that massive doses of potassium iodide which the patient accidentally received in 1953, may have contributed to his recovery.

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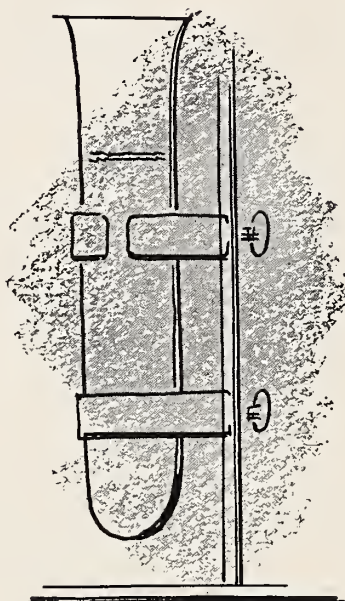
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# Partial and Total Pancreatectomy For Periapillary Carcinoma

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■ *Total pancreatectomy for periapillary carcinoma should be reserved for resectable primary carcinoma in the pancreas. The postoperative complications are reduced, and the resultant diabetes is not difficult to manage.*

*There were no postoperative deaths in series of 12 cases of total and partial pancreatectomy. This study proposes a more aggressive approach to malignant lesions in this area.*

PERIAMPULLAR CARCINOMA includes cancer of the head of the pancreas, the terminal end of the common bile duct, the ampulla of Vater and of adjacent duodenum. These lesions are similar to each other in many respects—in clinical manifestations, in the changes noted by laboratory determinations and in the approach and techniques of surgical excision. The prognosis, however, varies significantly, depending upon the site of origin.

Presented here are the reports of 12 consecutive patients who had radical resection on diagnosis of periapillary carcinoma. Four of the 12 had total pancreatectomy as part of the radical resection. There were no postoperative deaths.

In 1898, Halsted<sup>12</sup> performed the first transduodenal resection for an ampillary carcinoma; he did a wedge resection of the lesion and reimplanted the common bile duct and pancreatic duct into the duodenum. A cautious and conservative approach to this area persisted, for most surgical authorities believed that the pancreatic ferments

were essential to life and hesitated to widely resect the pancreas. It remained for Whipple<sup>21</sup> (in 1935) to design and present the classic two-stage operation for wider removal of a cancer of the ampulla of Vater.

Brunschwig,<sup>4</sup> in 1937, performed the first radical pancreaticoduodenectomy, and ligated the pancreatic stump. About 1940 a number of surgeons became optimistic and began performing a one-stage resection.<sup>20</sup> A period of pessimism followed, as most major centers showed a 20 to 30 per cent operative mortality; by 1947, no case of cure of cancer of the head of the pancreas had been reported.

A middle of the road course with reduced morbidity and mortality evolved, following increased experience in surgical techniques, in preoperative and postoperative care and in proper selection of patients. From the reports of others and their own observations, the present authors came to believe that a more enthusiastic team approach toward earlier diagnosis, wide field radical operation with total pancreatectomy in selected cases, and careful

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management of the metabolic alterations, will improve the present figures on survival and palliation.

### Reports of 12 Operations

Of 12 consecutive patients who had radical resection of the pancreas and duodenum, 11 had carcinoma—in the duodenum in two cases, the ampulla of Vater in two and the pancreas in seven. One of the 12 had benign duodenal ulcer with chronic pancreatitis. The patients were from 44 to 72 years of age. Six patients had pain in the epigastrium and jaundice. Total pancreatectomy was done in four patients, ligation of the pancreatic duct and oversewing of the end of the pancreas in six, and anastomosis of the pancreas to the jejunum in two others. A temporary pancreatic fistula developed in two of the patients who had ligation of the pancreas. There were no postoperative deaths.

Six of the patients are still living. The other six died at five (2), seven, eight, nine and 30 months after radical resection.

CASE 1. A 47-year-old woman with a history of epigastric pain, intermittent nausea and a weight loss of nine pounds over a period of one year was treated for duodenal ulcer, after which roentgenologic studies indicated a tumor of the second portion of the duodenum. In April of 1954, a radical pancreatico-duodenectomy and a 50 per cent gastric resection were done. The remaining pancreatic stump was ligated. There was no jaundice, and the common duct was small, so the gallbladder was anastomosed to the jejunum and the distal end of the common duct was closed. The removed specimen showed adenocarcinoma of the duodenum with lymph node metastasis. The postoperative course was uneventful and the patient was discharged about three weeks after operation.

A year and a half later, she began having episodes of chills, fever and jaundice and it was thought that the tumor had recurred. However, in April 1956 (two years after the Whipple operation) the abdomen was opened and there was no evidence of recurrence. The common duct, however, was packed with stones distal to the junction of the cystic and common ducts. The stones were obstructing the cystic duct, causing cholangitis and jaundice. They were removed and the distal end of the common duct was anastomosed to the jejunum. When last seen in April of 1964, the

patient was in excellent health without evidence of disease.

CASE 2. A 44-year-old man with a four-week history of upper abdominal pain was studied at the Cedars of Lebanon Hospital in May of 1954 and a tumor of the second portion of the duodenum was diagnosed by x-ray examination. At operation a hard mass was observed in the second portion of the duodenum. The head of the pancreas was "stony" hard, and the lesion was thought to be a carcinoma. Radical pancreatico-duodenectomy with a 30 per cent resection of the stomach was performed. The common duct, which was small, was ligated. The gallbladder was anastomosed to the jejunum. The specimen showed a large duodenal ulcer penetrating into the head of the pancreas with no evidence of malignant change. The postoperative course was relatively smooth and the patient was discharged three weeks after operation.

In September 1956, a little more than two years later, chills, fever and jaundice developed. X-ray examination at this time showed a definite marginal ulcer. At operation the marginal ulcer was observed and the distal common duct was found to be packed with stones (Figure 1) obstructing the cystic duct. Vagotomy was performed, the duct was cleared of all stones and the common duct was

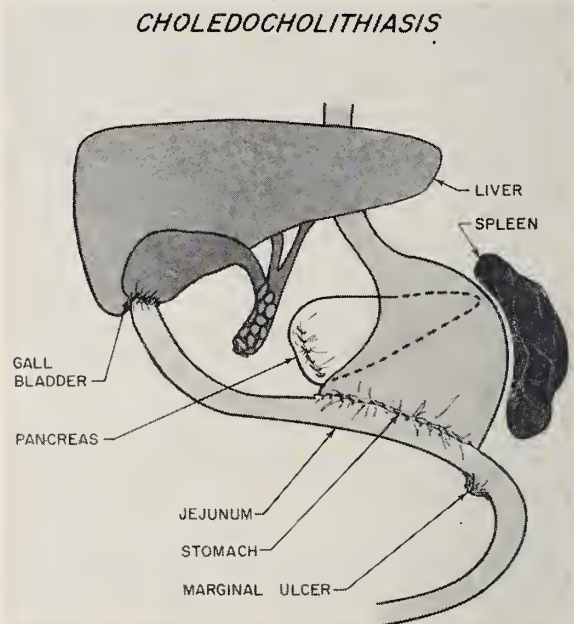


Figure 1.—Operative findings in Case No. 2 showing stones in the common bile duct cul-de-sac blocking the cystic duct, and a marginal ulcer.



anastomosed to the jejunum. When examined recently, the patient was found to be in excellent health.

CASE 3. A 47-year-old man was admitted with a history of intermittent upper abdominal pain of one year's duration, and of melena for one week before admission. A large mass in the second portion of the duodenum was demonstrated by x-ray. At operation January 1955, a large fungating tumor in the second portion of the duodenum contiguous with the head of the pancreas was observed. Radical pancreatico-duodenectomy was done and the stump of the remaining pancreas was ligated. The common bile duct was anastomosed to the jejunum. The pathologist reported myosarcoma of the duodenum with metastasis to regional lymph nodes and pancreas. The patient was discharged three weeks after operation. He did well until May, when evidence of recurrent tumor was noted. He deteriorated rapidly and died within a few weeks.

CASE 4. A 48-year-old woman was operated upon in October 1962 because of jaundice of short duration and a history of upper abdominal pain and backache which had been present for several months. A hard mass was found in the head of the pancreas and a radical pancreatico-duodenectomy with 50 per cent gastric resection was performed. The common duct, which was small, was ligated just below the junction of the cystic and common ducts and the gallbladder was anastomosed to the jejunum. The remaining portion of the pancreas was ligated. The specimen showed adenocarcinoma of the head of the pancreas with lymph node metastasis. The postoperative course was complicated by severe pancreatitis. A left pleural effusion developed, and the aspirated fluid had a high amylase content. A pancreatic fistula formed and drained through the incision. The patient finally recovered completely and did well until early in 1965 when liver metastasis became evident and she died in May 1965, two and a half years after operation.

A coeliac block for relief of intractable pain was performed about two months before death, with excellent palliation.

CASE 5. A 63-year-old woman with diabetes requiring 45 units of regular insulin and 80 units of NPH daily was operated upon in January 1963, because of severe obstructive jaundice. In x-ray studies with barium enema before operation, gall-

stones had been noted. The patient was thought to have benign obstructive jaundice. At operation, however, a tumor was found at the head of the pancreas, and pancreatico-duodenectomy was performed. Because of the severe diabetes, total pancreatectomy, cholecystectomy and a 50 per cent gastric resection were carried out. The specimen showed adenocarcinoma of the head of the pancreas with metastasis to lymph nodes. There were stones in the gallbladder.

The postoperative course was uneventful, the diabetes causing relatively little difficulty. For about eight months the patient did well, then she began to deteriorate rapidly and soon died with extensive metastasis to the liver.

CASE 6. A 47-year-old man was operated upon in September of 1961 because of a persistent painless jaundice which at first was thought to be due to hepatitis. A tumor was found in the ampulla of Vater, and a Whipple operation was performed. A 60 per cent gastric resection was done, the common duct was anastomosed to the jejunum, the gallbladder was removed and the remaining segment of pancreas was ligated. The specimen showed adenocarcinoma of the ampulla without evidence of lymph node metastasis. The postoperative course was complicated by a pancreatic fistula and gastrointestinal bleeding. The patient finally recovered and was discharged five weeks after operation. At last report, a year and a half after operation, he was in excellent health.

CASE 7. A 64-year-old man was operated upon in January 1965 because of progressive painless jaundice with weight loss and palpable enlargement of the gallbladder. He had had subtotal gastrectomy for duodenal ulcer eight years previously. Carcinoma of the head of the pancreas was found at operation, and a Whipple procedure with total pancreatectomy was carried out. The gallbladder was removed and the common duct was anastomosed to the jejunum. The pathologist reported cholecystitis and cholelithiasis with carcinoma of the head of the pancreas, but without lymph node metastasis. The patient was discharged on the eighth postoperative day. He was doing very well when last observed 14 months after operation.

CASE 8. A 68-year-old woman was operated upon in January of 1965 because of jaundice with a palpable gallbladder. At operation, a hard mass was felt at the head of the pancreas, and the

entire pancreas was indurated. A Whipple operation with total pancreatectomy and 70 per cent gastric resection was carried out. The pathologist reported undifferentiated adenocarcinoma in the head of the pancreas with involvement of the duodenal wall. Regional lymph nodes were not involved. The postoperative course was uneventful and the diabetes was controlled without difficulty.

In August 1965 the patient began to deteriorate rapidly and she died in September.

CASE 9. A 62-year-old man had a history of intermittent abdominal pain for seven years. In that time the only positive x-ray finding was a large, deformed duodenal loop which had been observed over a five-year period. He had been mildly diabetic for five years. Exhaustive diagnostic studies were entirely negative. With a provisional diagnosis of carcinoma of the pancreas because of the development of intractable pain in the epigastrium and back, operation was done in January 1955. A carcinoma of the pancreas was found and a Whipple operation with total pancreatectomy was performed. The pathologist reported carcinoma of the pancreas with extensive regional metastasis. The postoperative course was complicated by anuria, which responded to vigorous treatment. He was discharged three weeks after operation, with diabetes well controlled.

He was readmitted six weeks later because of recurrent intractable pain in the back. It was effectively relieved by a coeliac axis block with a phenol solution. The patient appeared to do very well following this procedure, but he died suddenly in May 1965 in a series of convulsive seizures due to cerebral metastasis.

CASE 10. The patient, a 52-year-old woman, had onset of jaundice and mild upper abdominal discomfort about a week before admission. A palpable gallbladder was noted on physical examination. A radiographic examination of the upper gastrointestinal tract showed no abnormality. Results of laboratory tests were compatible with an extrahepatic biliary obstruction. A Whipple resection was performed for carcinoma of the head of the pancreas. Total pancreatectomy was not done in this instance because the lymph nodes about the pancreas were clinically suspicious. The tail of the pancreas was oversewn and the gallbladder was anastomosed to the jejunum. The pathologist reported carcinoma of the head of the

pancreas with lymph node hyperplasia but no evidence of metastasis.

The postoperative course was uneventful and at last report, eight months later, the patient was doing well.

CASE 11. A 72-year-old female with a two-year history of upper abdominal pain was admitted for a cholecystogram, which showed cholelithiasis. Cholecystectomy was performed and the common bile duct was explored because of numerous small stones in the gallbladder. Cholangiograms showed a small filling defect near the ampulla of Vater, but a Hegar No. 7 dilator dropped into the duodenum easily. A lymph node was removed from behind the common bile duct and the duct was drained. The lymph node showed a focus of adenocarcinoma. Two weeks later a Whipple operation with anastomosis of the pancreatic body and tail to the open end of the jejunum was carried out. The pathologist reported adenocarcinoma of the ampulla without other evidence of metastasis. The patient was discharged two weeks after operation and when examined last, 15 months later, she was in excellent health with no evidence of recurrence.

CASE 12. A 47-year-old woman was operated upon because of painless jaundice and results of laboratory tests indicative of an extrahepatic obstruction. Conditions observed at operation suggested chronic pancreatitis and a specimen for biopsy was removed with a Silverman needle. After cholecystectomy and sphincterotomy, the wound was closed. The pathologist reported pancreatic ductal carcinoma. A week after the first operation a Whipple resection with anastomosis of the distal pancreas to the open end of the jejunum was carried out. The postoperative course was uneventful. The pathologist reported carcinoma of the pancreas without lymph node metastasis.

The patient was readmitted, moribund, six months later. The abdomen was greatly distended and the body temperature was 40°C (104°F). At operation a perforated marginal ulcer with peritonitis were observed. The patient soon died.

## Discussion

This presentation emphasizes the feasibility, in selected cases, of total pancreatectomy<sup>16</sup> along with the standard Whipple resection for carcinoma of the head, body or tail of the pancreas. Total



pancreatectomy is suggested when complete removal of all gross tumor appears feasible and the patient's clinical condition will tolerate a procedure of this magnitude. Removal of a primary tumor mass may add to the patient's comfort and subsequent nutritional status. The morbidity and mortality can be kept to a minimum with increasing experience, careful attention to technique and postoperative management.

Cole<sup>6</sup> found malignant cells from a carcinoma of the head of the pancreas floating throughout the pancreatic duct. The multicentricity of this lesion has also been shown in necropsy specimens. These two factors may contribute to the high local recurrence rate observed when only the head of the pancreas is resected. Removal of the body and tail of the pancreas does not add considerably to the operative procedure.

Dragstedt,<sup>9</sup> in his experimental work with dogs, showed that complete loss of pancreatic secretions through an external fistula will lead to ulcer formation in almost all cases. Ligation of ducts caused ulceration in almost one-third of the dogs, but total pancreatectomy was ulcerogenic in less than 2 per cent of the animals. The hyperglycemia that follows total pancreatectomy may have some protective effect on ulcer formation.<sup>17</sup>

One of the major complications after a standard Whipple operation is a pancreatic fistula with erosion and hemorrhage from adjacent organs. This is eliminated by total removal of the pancreas. In Waugh's series<sup>19</sup> (Mayo Clinic), postoperative pancreatic fistula developed in eight of 85 patients who had a Whipple operation.

In two operations in our series a postoperative pancreatic fistula developed. In both cases it closed spontaneously within two weeks and had little effect on the postoperative course. The material that drained from the opening was clear and produced very little skin excoriation. Both patients had had ligation of the main pancreatic duct and oversewing of the end of the pancreatic remnant.

This is in contrast to the serious fluid and electrolyte losses and skin erosion seen when a fistula develops at the anastomotic site between the pancreas and the jejunum. It appears probable that in fistulas of this type pancreatic ferments are activated by bile and enteric enzymes. It is on this basis that the authors recommend that, if pancreatectomy is not done, the pancreatic remnant be oversewn rather than anastomosed to the intestine.

The resultant diabetes following total pancreatectomy has been controlled without difficulty by proper titration with the various hypoglycemic drugs. A number of the patients who have this operation are already diabetic before pancreatectomy. There may be little change in the digestive processes, for in most cases considerable atrophy and fibrosis of the pancreas due to ductal blockage by tumor will have already taken place. Extracts of pancreas (Pancreatin and Viokase<sup>®</sup>) have nicely supplanted a physiologic need of the body for its digestive processes.

The approach in treating periampullary carcinoma has repeatedly changed in the 30 years since the article by Whipple<sup>21</sup> in 1935. The original article on the subject by Whipple described a procedure for surgical removal of an ampullary carcinoma. It has now been extended to include periampullary lesions, and a one-stage procedure is fairly routine. The patients are well prepared preoperatively and blood volume is restored to as nearly normal as possible.

The overall survival rate has not been good, as evidenced by data given in Fish's<sup>10</sup> collective review of 1,169 cases of periampullary carcinoma. The overall operative mortality was 19.9 per cent. Only 23 patients with pancreatic carcinoma, 51 with ampullary carcinoma, 13 with duodenal carcinoma and six with common bile duct carcinoma have survived longer than five years. In 1964 Judd<sup>13</sup> reported on a Mayo Clinic series of 347 cases of pancreatic carcinoma, in 316 of which operation was done. Five patients had a Whipple resection, one had a Whipple resection and total pancreatectomy, 148 had a palliative by-pass procedure and 162 had exploration only. The operative mortality rate was 30 per cent, and two of the six patients who had radical resection died postoperatively. Factors that led to a lesser operation, for palliation only, were pronounced obesity, fixation of the tumor, any possibility of distant spread or compromise of vital vessels.

Buckwalter,<sup>5</sup> in 1965, reviewed 349 cases of periampullary carcinoma and reported on 30 radical resections and 165 by-pass palliative procedures. The average survival was 21.8 months after radical resection, 5.8 months after by-pass only and 2.6 months after exploration alone.

The standard technique for pancreaticoduodenectomy has been described elsewhere.<sup>5,19</sup> Total pancreatectomy is not recommended for lesions arising in the common bile duct, the adjacent duo-



denum or the ampulla of Vater. The prognosis for extended life with malignant lesions arising in these sites is two or three times greater than that associated with carcinoma originating in the pancreas itself.<sup>18</sup>

When the sphincter of Oddi is removed, there is an upset in intrabiliary duct pressures, leading to stasis and gallstones. Unless the gallbladder is anastomosed to the intestine it should be removed. If the gallbladder is used in the anastomosis, and the common bile duct ligated, there is always the danger of disruption of the common bile duct suture line, and of bile peritonitis. This did not occur in our series. The common bile duct, if ligated, should be removed to within 0.5 cm of the cystic duct junction, lest stasis form in this cul-de-sac, as occurred in two of the cases herein reported.

The routine use of a gastroenterostomy when only a palliative biliary by-pass is done, is still not strongly advocated unless there is evidence of a possible early duodenal obstruction by tumor. More than 50 per cent of the stomach should be removed when the gastrectomy is carried out, for with a lesser amount a marginal jejunal ulceration may develop, as occurred in two patients in our series.

Radiation therapy and nerve blocks have helped in alleviating pain temporarily when lesions recur. Coeliac axis blocks<sup>2</sup> with alcohol or phenol have been very effective in several of the patients we have treated. Chemotherapy offers little, at this time, for pancreatic carcinoma but sporadic reports of temporary relief and improvement with 5-fluorouracil have appeared.

Although the series here reported is still early in follow-up and small in number, significant experiences have been presented. With earlier diagnosis and exploration, a higher survival rate may be achieved. We believe it is always well to be prepared for radical resection if the conditions observed at operation so indicate. We believe that radical operation is justified and we encourage the concept of wider field removal in an effort to control and remove the disease process.

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# The Management of Patients With Malignant Lymphoma

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■ *The prognosis of patients with malignant lymphoma discovered in the localized state and adequately treated is excellent. The prognosis for patients with malignant lymphoma, in general, is much more favorable than is generally recognized.*

*Radiation therapy is the treatment of choice for localized malignant lymphoma. Radiation therapy and chemotherapy can produce excellent palliation in patients with advanced disease and long-term survival in many of them.*

THE MALIGNANT LYMPHOMAS originate from the primitive mesenchyme. They occur universally, involve individuals of both sexes and all ages and may originate in most of the organs of the body.

Gall<sup>6</sup> defined malignant lymphoma as "an uncontrolled neoplastic overgrowth of one or another of the cellular inhabitants of lymph node tissue." He said further that it "is usually multinodal in distribution although often with regional limitation, and may on occasion arise in extranodal sites (viscera, skin, bone)."

A classification of the malignant lymphomas for treatment-planning is as follows:

- Lymphosarcoma
- Reticulum cell sarcoma
- Giant follicular lymphoma
- Hodgkin's disease

Jackson and Parker<sup>7</sup> have classified Hodgkin's disease into Hodgkin's paraganuloma, Hodgkin's granuloma and Hodgkin's sarcoma.

The cause of the malignant lymphomas is unknown. Because of the common origin of these tumors from the primitive mesenchyme, the growth may appear to be a variant of one type into another.

## Diagnosis

The diagnosis of malignant lymphoma is based upon the following criteria, as indicated:

- A complete history and physical examination.
- Biopsy of an entire lymph node whenever possible. It should be remembered that if lymph nodes are enlarged in several accessible superficial areas, the removal of a node from the groin or from the axilla is certainly less likely to be rewarding than the excision of an enlarged node from the neck. Because of repeated chronic infections or trauma to the extremities, the inguinal and axillary lymph nodes may often be enlarged.
- A roentgenogram of the chest, and, when indicated, a roentgenographic study of the gastrointestinal tract and of certain skeletal areas.
- A careful ear, nose and throat examination to rule in or out malignant lesions of other types.
- Peripheral blood studies and, if necessary, puncture of the sternum or ilium for bone marrow studies.
- Liver and kidney function tests and intravenous pyelograms when indicated.
- Lymphangiographic study may be done. This procedure will be especially helpful to determine the stage of the disease.

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## Basic Principles of Therapy

Some basic principles to be considered when deciding whether to use radiation therapy in the treatment of cancer are as follows:

- The cell type of the tumor to be treated.
- The anatomic location of the tumor and the extent or stage of the disease.
- Whether cure is possible or if only palliation is to be achieved.
- If cure is possible, whether to use surgical or radiation therapy singly or in combination.
- Knowledge of the use of other treatment measures, such as chemotherapy and hormone therapy, and the indications for them.
- A thorough knowledge of the life history of the disease to be treated.

It should be noted further that the knowledge, training and judgment of the therapist is more important than the type of equipment or the drugs to be used.

## Radiosensitivity

The malignant lymphomas as a group are radiosensitive. The most sensitive cells in the peripheral blood are lymphocytes, polymorphonuclear leukocytes and erythrocytes, in that order. Lymphoid tissue is very radiosensitive. Often lymphomas will regress after a tumor dose of 500 to 1,000 rads; however, recurrences are more frequent and at shorter intervals.

Noetzli and Sheline<sup>14</sup> made a study of local recurrence in lymph nodes irradiated for Hodgkin's disease. Their data indicated that in patients with this disease observed up to two years after radiation therapy, lymph node enlargement recurs more frequently and sooner after treatment with low doses than with higher doses. This relationship continued to tumor doses of approximately 2,000 rads.

Radiosensitivity and radiocurability are not necessarily synonymous; however, the possibilities for prolonged survival and a relatively high percentage of cure place the malignant lymphomas in a favorable group for radiation therapy.

## Therapy Equipment

The majority of malignant lymphomas have been treated by conventional x-ray therapy equipment (200 to 300 kv).

Since cobalt 60 and other types of megavoltage equipment have become more widely available, there has been a trend to use them in the treatment of the more deeply located lesions.

The advantages of megavoltage therapy are the sparing of the skin, greater depth doses can be more easily obtained, the radiation beam can be more precisely determined with less back and side scatter, and the radiation is absorbed more homogeneously throughout the entire treatment area because the difference in the rate of absorption in bone, fat and muscle is less than with conventional x-ray. Because of this more equal absorption in all tissues the dosage can be more accurately determined in the head and neck and pelvic and retroperitoneal regions where bone, soft tissues and air spaces are present.

It must be emphasized that it is not the radiation per se or the type of equipment that determines the outcome for the patient; what is essential is that the physician who is employing radiation therapy be well trained in its use, that he have an excellent knowledge of the life history of the disease to be treated and that he know the limitations of his own specialty and that of other specialties. He must also have an optimistic outlook, for too often a defeatist attitude will lessen the possibility of favorable outcome.

## Hodgkin's Disease

In order to plan the treatment for Hodgkin's disease, it is necessary to stage or classify the disease as to its extent. The method used at the Toronto General Hospital is as follows<sup>16</sup>:

Stage I—Involvement of a single site or lymphatic region.

Stage II—Involvement of two or three proximal lymphatic regions:

(a) Without symptoms of generalized disease;

(b) With symptoms of generalized disease.

Stage III—Involvement of two or more distant lymphatic regions.

Boden<sup>5</sup> advocated the treatment of all localized cases of lymphosarcoma and Hodgkin's disease according to the following principles:

"1. The zone to be treated must extend five cm wide in every direction of the lesion or of the lymph node group if the lesion lies in lymph nodes.

"2. The whole of the anatomical lymph node



group or groups associated with a lesion must be included in the zone to be treated.

“3. The zone must be irradiated as one undivided volume.”

Using the above principles for treatment, Bodin obtained a crude survival rate of 53 per cent for localized Hodgkin's disease and of 50 per cent for localized lymphosarcoma. His survival rate for five years for 112 patients with Hodgkin's disease was 26 per cent, and for 95 patients with lymphosarcoma it was 28 per cent.

The therapy of Hodgkin's disease has been very confusing. Often in the past only moderate doses of radiation therapy were given to patients with localized disease and the contiguous areas were seldom treated. The accepted opinion was that the disease was of multicentric origin and that the possibility of cure was minimal. Often patients with involvement of the mediastinal lymph nodes have been treated with small doses and not long afterward the nodes enlarged again and symptoms recurred. Many physicians have had a defeatist attitude toward the prognosis in patients with malignant lymphomas and some have expressed doubt that involvement is ever unicentric in this disease. Yet many of the patients with localized disease are young and have few if any systemic symptoms, and thorough treatment of the involved area, with prophylactic radiation therapy to adjacent lymphatic drainage areas, has certainly proven to be worthwhile.

Not often (until the terminal stage of the disease) are there recurrences in areas that have been heavily irradiated. In this regard it should be noted that it may take three months or more for the full effect of the therapy to be realized; hence one should not be in a hurry to re-treat an area because of enlargement of nodes.

If the disease is localized and radical operation is done, radiation therapy should not be given. The decision to be made is between adequate radiation therapy and surgical removal.

Vaeth<sup>19</sup> studied 45 cases of Hodgkin's disease in which mediastinal recurrence followed radiation therapy. This study confirmed the observation that failure is usually due to insufficient tumor dose or too small a field of treatment. He held that the entire bloc of mediastinal lymph nodes should receive at least 3,500 r tumor dose and that when adjoining fields are treated there should be no untreated areas between the fields.

Peters<sup>16</sup> advocated a dose of approximately

3,500 rads in three weeks to the involved area and 2,500 rads in three weeks to contiguous areas for Stages I and II.

Kaplan's<sup>9</sup> experience indicated a significant superiority of the intense treatment method, which consists of tumor doses of 3,500 to 4,000 rads in three to four weeks for localized Hodgkin's disease. The tumor dose is usually given to fields which include clinically uninvolved contiguous lymph node chains, with or without concomitant nitrogen mustard treatment.

Crosbie<sup>4</sup> recommended a tumor dose of 3,500 to 4,000 r when Hodgkin's disease is limited to a single set of lymph nodes. When the disease involves two or three contiguous lymph node groups, a similar tumor dose is given and, in addition, the uninvolved contiguous lymph node groups are prophylactically treated.

Peters<sup>15</sup> reported long-term survival rates of 319 patients with Hodgkin's disease treated by radiation in the period 1928-54 as follows:

Stage	Number of Patients	Survival			
		5 Year	10 Year	15 Year	20 Year
I .....	70	71%	50%	40%	40%
IIa ....	51	88%	66%	50%	50%
IIb .....	63	22%	10%	3%	0%
III .....	135	14%	5%	4%	2%
All Stages ...	319	40%	26%	20%	18%

Five-year survival rates for 316 patients with Hodgkin's disease reported by Molander and Pack<sup>11</sup> were 37.5 per cent for those with Stage I disease, 27.5 per cent for Stage II and 14.8 per cent for Stage III. These investigators were of the opinion that radiation therapy is the principal and most effective form of treatment for the majority of patients with malignant lymphoma.

### Hodgkin's Disease in Children

In children Hodgkin's disease confined to lymph nodes in one region may be curable by radiation therapy the same as in adults. Kelly<sup>10</sup> reported that in 32 of 42 cases in children under 15 years old, enlargement of cervical lymph nodes was the presenting symptom, and it was the main symptom in 27 of 28 patients with localized disease. Twelve of the 42 patients were alive and well five years after radiation therapy and eight of the 30 who died survived at least five years.

Pitcock<sup>17</sup> and associates in a study of 46 children with Hodgkin's disease, all but one treated principally with irradiation, found that 60 per cent

with localized disease lived five years and 35 per cent for ten years. Eight of the 46 (17 per cent) were still alive from five to 33 years after the diagnosis, which was made by biopsy. These investigators found that initial doses of radiation therapy less than 1,800 r in Stage I (localized) cases did not completely eradicate the disease and retreatment of the lymph node area was necessary.

Peters and Middlemiss<sup>16</sup> reported the five-year survival of 11 children under 11 years of age with Hodgkin's disease treated by radiation therapy as 55 per cent and for 27 patients with ages ranging from 11 to 20 years as 52 per cent.

While the disease is more common in males, the prognosis is more favorable in females.

No data has been presented to show that radical operation alone will produce better results than radiation therapy. Operation usually is limited to the taking of an intact large lymph node for histological study.

### Malignant Lymphoma Other Than Hodgkin's Disease

If a patient has localized lymphosarcoma or reticulum cell sarcoma, the same kind of therapy as that used for Hodgkin's disease should be carried out. The prognosis is better, however, with Hodgkin's disease and the lesions grow more slowly.

Fuller<sup>5</sup> found that tumor doses of approximately 3,000 to 5,000 rads are necessary for permanent control of malignant lymphomas of Stage I and Stage II. She expressed the opinion that reticulum cell sarcomas generally require a tumor dose of about 5,000 rads. The lymphocytic lymphosarcomas are more radiosensitive. She administered prophylactic radiation therapy to the supraclavicular fossa when the disease originated in the mediastinum or the axilla. Of a series of 278 patients with malignant lymphomas, 38.4 per cent survived for five years.

The results of treatment of 567 patients with malignant lymphoma other than Hodgkin's disease are reported by Molander and Pack<sup>11</sup> as follows: Five-year survival for Stage I was 35 per cent, for Stage II 25 per cent, and for Stage III 22 per cent.

### Chemotherapy

There is no indication for the use of chemotherapy in the treatment of localized (Stage I) Hodgkin's disease or of Stage IIa. Patients in

Stage IIb who have systemic symptoms might be helped by chemotherapy in addition to irradiation. The initial approach to the therapy of patients with Stage III involvement could be by chemotherapy, with irradiation used for residual lesions. The chemotherapeutic agents most commonly used in the treatment of the malignant lymphomas are nitrogen mustard (HN<sub>2</sub>), cyclophosphamide (Cytosan®) and thio-tepa. The chemotherapeutic agents are palliative, not curative.

Radiation therapy alone or with chemotherapy can produce effective palliation of hepatosplenomegaly, bone lesions, paraplegia, and symptoms caused by involvement of other organs.

### Gastrointestinal Malignant Lymphoma

Jordan and coworkers,<sup>8</sup> in a review of the English literature on gastric malignant lymphomas in the period 1939-1954, collected reports of 406 cases. Detailed analysis was available on 373 cases of primary lymphoma of the stomach. Among patients who survived resective operation, the five-year survival rate was 42.6 per cent. In comparing the end results of the treatment of primary lymphomas of the stomach with gastric carcinoma, they concluded that the prognosis for gastric lymphoma was twice as good as the best reported five-year survival rates for gastric carcinoma. They recommended radiation therapy for all patients with lymphoma who had any residual disease after operation.

A survival rate of 42 per cent in 24 patients who had operation for primary gastric malignant lymphoma was reported by Warren and Littlefield.<sup>70</sup>

Cook and Corbett<sup>3</sup> in reporting on 1,014 cases of malignant lymphoma noted that 6.5 per cent of the cases were primary in the gastrointestinal tract with the majority being lymphosarcomas. The absolute five-year survival rate for 42 cases of lymphosarcoma and reticulum cell sarcoma originating in the gastrointestinal tract and mesentery was 35.7 per cent. Cook and Corbett expressed the opinion that "while surgery provides a valuable adjunct in the management of their patients, roentgen therapy remains the indispensable treatment for both localized and generalized lymphoma."

Twenty-nine per cent of 21 patients with primary gastric malignant lymphomas treated at the Memorial Hospital for Cancer and Allied Diseases, New York City, lived for five years or



longer. McNeer,<sup>12</sup> who reported on this series, commented that "although primary gastric Hodgkin's disease has been described and reported by some authors, the senior pathologists at Memorial Hospital do not believe that Hodgkin's granuloma ever appears as a primary gastric tumor." Lymphocytic lymphosarcoma and reticulum cell sarcoma were the lymphomatous types reported by McNeer.

In a series of patients with malignant lymphomatous involvement of the small bowel reported upon by McPeak,<sup>13</sup> the one patient with lymphosarcoma of the duodenum who was treated surgically did not survive five years. Radiation therapy was used before or after operation in eight patients with jejunal lymphosarcoma and four of them had some palliative effect. Chemotherapy, used in three patients, was without benefit. There were no long-term survivors. Of 18 patients with lymphosarcoma of the ileum, 15 had postoperative radiation and in five of them it had some palliative effect. Of seven patients who received chemotherapy, three had some transient effect. Three patients with ileal lymphosarcoma who were treated with irradiation after operation were alive and well for five years.

Ullman and Abeshouse<sup>18</sup> collected reports of 109 cases of lymphosarcoma of the intestines and found that in only 32 of them did the lesion originate in the large bowel.

It is often difficult for a surgeon to differentiate accurately between a gastrointestinal malignant lymphoma and a primary carcinoma solely from visual inspection and palpation. Biopsy studies should always be made because if the lesion is considered to be inoperable, radiation therapy may at least be palliative and possibly curative. In any case in which resection of the lesion is considered not to have been adequate or disease is present in the regional lymph nodes, radiation therapy should be carried out.

### Hodgkin's Disease and Pregnancy

Considerable scientific evidence has been accumulated to indicate that the course of Hodgkin's disease is not influenced by pregnancy nor the fetus adversely affected. For this reason therapeutic abortions have not been recommended.

All therapy should be avoided during the first trimester of pregnancy because of the potential danger of fetal injury. When therapy of any type is given, the possibility of harmful effects to the

fetus should be considered. I treated one patient with Hodgkin's disease who had four children in the 12 years she lived after diagnosis of Hodgkin's disease. Fortunately at times when the disease became active during pregnancy, the affected area was such that treatment could be postponed until after delivery.

Becker and Hyman<sup>1</sup> determined the amount of radiation which would reach the fetus from internal scatter. When a tissue dose of 1,000 r was delivered to the mid-mediastinum through a 15 × 15 cm field, the internal scatter to the fetal region was 9.0 for 250 kv radiation; 2.9 r for cobalt 60; and less than 0.1 r for rays from the 22.5 Mev betatron. The external scatter which could be reduced by shielding of the abdomen by appropriate material was found to be less than 0.1 r for all three treatment modalities.

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# Small Bowel Obstruction Due to Intramural Hematoma During Anticoagulant Therapy

## *A Non-Surgical Condition*

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■ *Intramural hematoma of the small bowel should be suspected in any patient with signs or symptoms of small bowel obstruction who is having anticoagulant drug therapy, especially if it is long-term therapy and if the prothrombin time is excessively prolonged. A barium study is indicated and if the roentgen pattern is characteristic, conservative treatment is indicated. Unless there is an associated abdominal lesion requiring operation, most patients will improve in four to six days. Those not improving usually have other complicating conditions.*

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SMALL BOWEL OBSTRUCTION due to intramural hematoma is a rare clinical entity. Before anticoagulant drug therapy, about 25 instances were reported, most of them resulting from trauma.<sup>23</sup> Since anticoagulant drug therapy, however, a total of 35 reports have been collected, 33 of them in the last eight years.

Before 1961, the cause of the obstruction was uncertain and early laparotomy was considered indicated. Abdominal cramps, nausea, vomiting and distension of the small bowel as visualized on a plain roentgenogram led to the diagnosis of small bowel obstruction in 17 of 18 recorded patients.<sup>2,4,7-10,15-20</sup> Barium by mouth seemed contraindicated in the presence of mechanical obstruc-

tion. Intramural hematomas of the small bowel were found at laparotomy.

Culver and coworkers,<sup>5</sup> however, in 1961, showed by barium studies that the distension was caused by an intramural hematoma. He demonstrated the same "coiled spring" pattern previously considered pathognomonic for intramural hematoma due to trauma<sup>6,14</sup> (Figure 1). This was confirmed by Wiot and coworkers<sup>24</sup> and Senturia and his associates,<sup>21</sup> who described an additional "spiked" or "picket fence" pattern, equally pathognomonic (Figure 2).

Since then barium studies have been done in 17 patients. A diagnosis of intramural hematoma was made in 16 patients, and of diverticulitis in one.

An analysis of these 35 reports indicates that intramural hematoma of the small bowel uncom-

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Figure 1.—Intramural hematoma of duodenum. Arrows indicate "coiled spring sign." Duodenum is dilated and barium coils are in the grooves formed by adjacent mucosa elevated by hemorrhage. Patient had thrombocytopenic purpura. In some instances, identical findings are associated with direct trauma such as from a bicycle handlebar. (From Brodeur, Armand E.: *Radiologic Diagnosis of Infants and Children*. The C. V. Mosby Company, St. Louis, 1965. Reprinted with permission of the publisher.)

plicated by other intra-abdominal pathologic conditions will subside with conservative treatment. Laparotomy is not indicated.

### Diagnosis

The recognition of intramural hematoma from anticoagulant drugs as a clinical entity is vitally important in prevention, diagnosis and treatment. First, it is preventable by better management, inasmuch as nearly all hemorrhages have occurred with excessive hypocoagulability. Second, when suspected, it is diagnosable early with safety by barium study of the small bowel. Third, the mechanical obstruction which it may produce is the only type which invariably is reversible by conservative treatment. Fourth, operative intervention, then, is contraindicated unless there is an associated intra-abdominal lesion for which an operation is indicated. This rarely occurs. These points have been stressed by other investigators<sup>9,20,22</sup> but need further emphasis.

### Natural History

Clinicians, surgeons, pathologists and roentgenologists all contributed in elucidating the natural

history and the proper treatment of this entity. Berman and Mainella,<sup>2</sup> who were the first to describe this disease entity, noted abdominal cramps, vomiting and a plain roentgenogram showing pronounced distension of the proximal loop of the small bowel. At laparotomy, the surgeon found that a "sausage shaped mass, 10 inches long, in the lower jejunum was hemorrhagic and black in color." The segment was thought to be necrotic and was resected but the pathologist reported that "microscopic examination through the intestinal wall revealed a normal mucosa as well as muscularis."

### Reported Cases

To the 34 reported instances of intramural hematoma of the small bowel occurring during anticoagulant drug therapy, I am adding one. The record of this case was discovered by inquiry at the roentgenology department of St. Vincent's Hospital. Certain instances of paralytic ileus associated with anticoagulant treatment may have been due to intramural hematomas but were not verified and were excluded.<sup>1,9,11,19</sup>



Figure 2.—Intramural hematoma of the jejunum, rigid, thickened mucosal folds and narrow barium-filled spaces between them simulating a picket fence. (From St. Vincent's Hospital, Department of Radiology, Los Angeles.)



The 35 patients may be grouped as follows: Group 1—18 of the first patients, most of them seen before Culver demonstrated the safety of barium by mouth<sup>5</sup>; Group 2—17 patients who had barium study.

Patients in Group 1 had only plain roentgenograms and all but one were considered to have intestinal obstruction of uncertain origin. The intramural hematomas were diagnosed at laparotomy. In 15 patients, the bowel was considered nonviable and a segment was resected. Of the remaining three, volvulus was found in one, complicating the hematoma, and was released. The bowel was found to be viable after application of warm packs, and was not resected.<sup>16</sup> The patient recovered. In the other two cases the hematoma was in the terminal ileum, and enteroanastomosis was performed in one<sup>19</sup> and ileocolostomy in the other.<sup>3,10</sup> The first patient died of staphylococcus septicemia after five weeks. At necropsy, the bowel appeared healthy. The second patient died of peritonitis after five days.

Although the intestinal segment was resected in 15 patients, the reports did not state what tests were applied at laparotomy to establish nonviability. In some cases, absence of peristalsis in the hemorrhagic segment was considered adequate evidence<sup>7,8</sup> but the resected segments were not found to be necrotic. The apparent urgency of operation is indicated by the fact that all of the 18 patients were operated on within four days of onset of symptoms.

In Group 2—the 17 patients with barium studies—a diagnosis of intramural hematoma of the small bowel was made in 16 cases, and of diverticulitis of the jejunum in one. These 17 may be divided into two groups: 11 patients who were treated conservatively and recovered, and the other six patients who, although the primary diagnosis in five was intramural hematoma, were operated on because of the possibility of a mistaken diagnosis. One patient was operated on within 24 hours because of the possibility of segmental intestinal infarction. Four were “clinically improved” or “asymptomatic” at the time of operation 4, 10, 12 and 16 days after entry to the hospital. The appearance of a mass, or persistence of x-ray distortion, or the fear of small bowel cancer or infarction, led to laparotomy despite clinical improvement.<sup>5,16,22</sup>

The sixth patient<sup>21</sup> was the only one not clinically improving after four days of conservative

treatment. The first diagnosis had been adynamic ileus, but it was changed to incomplete mechanical small intestinal obstruction due to continued distension of the small intestinal loops. A barium study then showed the typical roentgenographic “spiked pattern” of intramural hematoma (Figure 2). Instead of improving, however, the patient became decidedly worse on the fourth hospital day and “because there was no improvement in the clinical condition, laparotomy was performed.”

A perforated appendix with localized abscess formation was found, and there were two segments of thickened hemorrhagic small bowel. One segment was resected. Nineteen days later, a barium study of the small intestine showed the other intestinal segment to be normal. All six of the patients in this group lived.

Of the total of 35 patients, 24 had laparotomy and 11 had conservative treatment. Four of the 24 patients who had laparotomy died, three probably as a result of the operation.<sup>10,15,19</sup> The other patient died 14 days after operation of acute myocardial infarction.<sup>20</sup> None of the 11 patients treated conservatively died.

In 25 cases the hematomas were in the wall of the jejunum, in six in the ileum and in four in the duodenum.

Nearly all of the patients, 32 of 35, were receiving long-term anticoagulant therapy. A period of treatment over six weeks was considered long-term. The shortest term of treatment was 14 days, the longest seven years. Eight patients had been under treatment a year or longer and the others, with three exceptions, for at least six weeks. In the 32 cases in which the prothrombin activity was given, the prothrombin levels were outside the desirable range. Most patients' blood showed excessive hypocoagulability.

Seventeen patients were being treated for myocardial infarction, eight for “coronary artery disease,” six for cerebral vascular disease, two for endarteritis and two for systemic arterial embolism.

### Indications for Laparotomy

In 18 patients, laparotomy was done because of abdominal pain, vomiting, distension and plain roentgenographic evidence of small bowel obstruction. After the studies of Culver,<sup>5</sup> Wiot<sup>24</sup> and Senturia,<sup>21</sup> the specific diagnosis of intramural hematoma of the small bowel was made possible and conservative treatment was advocated.

The appearance of the bowel at laparotomy was described variously, as follows: "hemorrhagic . . . sausage-shaped mass,"<sup>2</sup> "thickened, edematous,"<sup>5</sup> "bluish segment,"<sup>22</sup> "red swollen bowel,"<sup>19</sup> "violaceous,"<sup>9</sup> "reddish black jejunum oozing blood."<sup>13</sup>

The length of the hemorrhagic segment involved varied from 10 centimeters<sup>18</sup> to the entire length of the jejunum.<sup>5</sup> Free blood in the peritoneal cavity was mentioned in 16 instances. The amount varied from 200 to 2,000 ml and the average was 400 ml.

In none of the resected segments was there microscopic evidence of necrosis. The mucous membrane, the first tissue to suffer from vascular insufficiency, was intact in all cases. In two instances, there were areas of superficial focal mucosal erosion but no necrosis.<sup>7,10</sup>

## Discussion

These reports indicate that the only reliable procedure to diagnose intramural hematomas of the small bowel from anticoagulant drugs is barium study. This is a safe procedure if the obstruction is caused by anticoagulant drugs, in contrast to the mechanical obstructions of other types.

Conservative treatment usually leads to improvement within four to six days, with eventual resolution of the hematoma. The hemorrhagic bowel is not necrotic and recovers normal function under conservative treatment. In the 20 resected segments of bowel, pathologists found no necrosis. In the patients operated on, in whom the bowel was not resected, the hematomas resolved.<sup>5,16,19,21</sup> Furthermore, when hematomas were diagnosed by roentgenogram and operation was not done, later barium studies showed a return of normal bowel function. Early fears that scarring and narrowing of the lumen of the small bowel would occur were not justified. In six instances, the roentgenographic pattern was shown to return to normal in two to six weeks of conservative treatment.<sup>13,21,24</sup>

When barium x-ray studies are not done early, the hemoperitoneum which usually accompanies intramural hematoma of the small bowel may be diagnosed by paracentesis and attributed to a ruptured aneurysm.<sup>3</sup> In other instances, intestinal obstruction may be interpreted as secondary to hemoperitoneum.<sup>12</sup>

Several points are not understood. It is not clear why the jejunum should be the site of predilection for intramural hematoma of the small bowel due to anticoagulant drugs, whereas it is the duodenum

that is the most often affected if the hematoma is induced by trauma. Also, associated major or minor bleeding cannot be relied upon to indicate intramural bleeding. Obvious bleeding may be absent. Gross hematemesis occurred in only nine of the 35 reported cases, gross melena in only six. Minor hemorrhage occurred in only 14. Ileus, during anticoagulant therapy, has been shown to respond to conservative treatment, regardless of the site of the hemorrhage causing the ileus.<sup>11</sup> It is important to identify the causative lesion, if possible, however, because if it be intramural hemorrhage of the small bowel it is a continuing vulnerable area and if anticoagulant therapy is begun again, recurrent intramural hematomas may develop, as has happened in some cases.<sup>9</sup>

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## ADDENDUM

Several reports either overlooked or appearing since this was written have not changed the deductions of this paper:

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# Community Mental Health

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■ *The distinctive feature of a community mental health program is the comprehensive responsibility assumed for the mental health as well as the psychiatric needs of a particular area. Not only must programs provide psychiatric services but, in addition, they are concerned with assessing the community's psychiatric and mental health status; with preventive services; with mental health education; with contributions directed toward the solution of certain social problems; as well as with a variety of other indirect services, including, importantly, mental health consultation. This form of consultation can support and help the large number of community caretakers whose contribution is vital to the promotion of community mental health.*

THE RESPONSIBILITY for a specific population is the distinguishing characteristic of community mental health practice, and it is this shift of attention from concerns with the individual to the mental health needs of a community that establishes the uniqueness of the field. This responsibility extends not only to planning services for and treating members of the population who demonstrate or in some way acknowledge the presence of emotional problems, but, in addition, it also encompasses persons who are emotionally disturbed but unaware of their problem and whom the current, existing methods of psychiatric treatment are not reaching. This comprehensive responsibility pertains broadly to all ages, all types of problems, all cultural and racial groups and the members of every socioeconomic class. To further compound this responsibility, the charge is not only to provide the necessary psychiatric treatment but also to establish programs for the prevention of disease and the promotion of the mental health of the population.

In this field, a variety of social issues and problems of community living inevitably become particular concerns. These include (to cite only a few

examples) alcoholism, suicide, drug addiction, delinquency, mental retardation, housing, poverty, unemployment and racial intolerance.

It is not surprising that this range of challenging responsibilities assigned to the community mental health field currently remains an unachieved ideal for most programs and that various critics have labeled these goals as grossly unrealistic, socialistic or not within the domain of legitimate mental health practice. Not ignoring the seriousness of these charges and concerns, programs continue to increase in number and importance throughout the country.

This is still a new and rapidly developing field and even the boundaries of the various subdivisions of practice remain somewhat blurred. Many people look upon *community psychiatry* and *community mental health* as synonymous terms. Others visualize community mental health as being the broader designation which includes within its scope the separate area, community psychiatry, which is primarily concerned with the treatment and management of the materialized psychiatric disorders of a community by the psychiatric professional team. From this viewpoint, community mental health is perceived as being concerned with mental health as well as mental illness, with prevention as well as psychiatric treatment; and the designation of community mental health perhaps more clearly underlines the important contribution that is

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made in this field by non-psychiatric professionals and laymen. Social psychiatry is generally regarded as having more of a research, study and theoretical orientation, as being less of an applied field than community mental health, and as concerning itself with social problems and the relevance of social system functioning to a population's mental health.

The types and sizes of communities that may constitute a "population responsibility" in the practice of community mental health are varied. In general, the boundaries of the particular community are established by geographic or functional determinants. From the geographic dimension, the community may be specified as a city, a county, a region of a state, an entire state or, in some contexts, the entire nation. *Function* can delineate populations and communities for special programs—an industrial firm, for example, or a college, an army unit or a trade union.

The responsibility of a community mental health program for a particular population is generally established by a formal contract or a job assignment of one kind or another. This may originate out of separate or combined federal, state or local community mental health service legislation or through private contracts. Each contract should detail the responsibilities to be assumed. Obviously, programs are not imposed upon communities. Rather, all community programs should originate from the population's request for services, and the success of any program will be determined by the community's continued interest and participation in the planning and operation of the enterprise.

The major responsibility assumed by any community mental health program is the charge to reduce the incidence of mental disorder in the population as well as to decrease the amount of disability and defect resulting from mental illness.

At present there is no tried and validated model program or approach which has demonstrated that it can conclusively accomplish a reduction in the incidence of mental disorder in a community. Indeed, psychiatry in general lacks this type of validated evidence for the effectiveness of its treatment approaches. But a significant amount of research and study is being conducted, and it may be that at some future time a validated program model for community mental health intervention will be available. It may be well to mention here that mental health professionals are not maintaining that they have available answers or solutions to

the numerous social problems confronting communities or that these eventual solutions will necessarily call for contributions from the field of mental health. The mental health profession in general remains as unsure about coping with these issues as are any of the other agencies and individuals in the community. Above all, there is no wish to contaminate the important helping roles of teachers, police, social agencies and many other community workers by having them assume a pseudopsychiatric stance. However, a responsibility clearly remains to be interested in, concerned about and actively participating with others in exploring possible approaches and solutions to these important problems.

The acknowledged absence of a validated approach for lowering the incidence of mental illness in a community does not mean that we lack programs which can with considerable conviction be recommended to communities, nor does it warrant waiting to move into community mental health planning until the tested model emerges. Rather, the present situation necessitates that introduction of programs, program evaluation and community-based mental health research be conducted concurrently.

To describe the various activities and services that would be included in an "average" community mental health service program would be an exhausting assignment. Perhaps it will suffice to note that these responsibilities generally fall into the following very broad and obviously comprehensive categories:

- Activities relating to the assessment and definition of the particular community's mental health needs and the maintenance of a continuing functional record of information and data.
- Direct treatment services to the identified psychiatric patients in the population.
- Indirect consultative services designed to support and assist various community caretakers in their work, which is of great importance to the mental health of the community.
- Services and programs whose goals are the prevention of mental illness as well as the promotion of mental health or mental health education.
- The services and contributions the program provides with reference to special social and community problems perceived as being intimately related to mental health or mental illness.

- The various administrative, coordinative and program evaluation systems necessary for the successful operation of the program.
- Professional and non-professional training.
- Research programs of all types.

The psychiatric treatment offered by the direct service component of community mental health programs characteristically emphasize a crisis or a short-term therapeutic approach. The goal of the therapy is the resolution of a current crisis or disequilibrium with a quick return of the patient to a functional role in the community. The treatment goals advocated by most programs, which by now verge upon professional slogans, include:

- Psychiatric treatment available at the point in time when the problem presents.
- Treatment within the environs of the individual's familiar neighborhood and community.
- Availability of the variety of different types of service as needed—that is, comprehensive care. Included, therefore, should be opportunities for 24-hour care, day hospital programs, outpatient and emergency treatment, and a number of transitional and after-care programs. To construct such a network of comprehensive care requires that private or public treatment components already operative in the community be creatively involved and utilized in the mental health program.
- Insure continuity of professional team members and familiar helpers throughout the course of treatment, irrespective of the different approaches employed.
- Return the patient to a functional role in the community at the earliest opportunity.

The preventive components of community mental health programs electively focus upon individuals at special risk in the population who may become "targets" for particular services or attention. Predictable life crises and maturational stresses help to identify these individuals in the community. These points of potential emotional disequilibrium cover a wide range of experience, including, for example, serious illness, surgical operation, pregnancy, premature birth of an infant, marriage, death of a family member, induction into the Armed Services or the Peace Corps, or relocation or retirement. The appropriate "helping" interventions for these different crises are varied, ranging from observation, support, providing certain supplies, education, anticipatory guidance,

encouraging social organization or action, consultation with other helpers or crisis therapy. Those directing programs must also be alert to noxious or harmful factors which may contribute to mental illness, including awareness of various social, cultural, economic and legal factors of stress as they impinge upon the community.

In most programs, small professional staffs will be confronted with an overwhelming responsibility. Therefore, those responsible for each program must determine how to best address their efforts to this assignment. Traditionally, the community expects that mental health programs will provide direct diagnostic and psychiatric treatment services to persons in need. However, initially a significant amount of attention may be devoted to determining what psychiatric and non-psychiatric helping agencies, groups and individuals are already dealing with these problems. Mental health programs may be started with the provocative position that it is essential that none of these helping agencies relinquish their current roles in the mental health complex. Rather, these groups are asked to consider how the mental health services program might help them in their continued shouldering of this responsibility.

Frequently, when activities of these programs are shared and reviewed, it is mutually concluded that the mental health needs of the client are being met and that direct treatment intervention of the mental health team is not indicated. In this way, a pattern may be established whereby various community groups who have an important first-line relationship with individuals in crisis, in emotional conflict or in psychiatric illness turn to the mental health program, asking to *confer* about their "problem" rather than requesting that their clients receive psychiatric treatment. The caretakers who request services from the *mental health consultation* division of a community program may include, for example, the police, lawyers, public health nurses, social workers, the clergy, educators and the schools, hotel operators, housing project officials, probation officers, general physicians, welfare departments and employment counselors.

Briefly, the goal of mental health consultation described by a number of authors<sup>1,2,3</sup> is to help these community caretakers in their current work with their clients, many of whom have serious psychiatric problems. When a worker from an agency or community program consults with a mental



health professional, he is, if the consultation proves helpful, acquiring understanding and skill in dealing with a number of cases which can be anticipated to come his way in the future. Herein lies the relevance, the importance and the economy of the mental health professional's investment in the consultation service. The consultant focuses upon problems that the person consulting him is having in work with his client. From the consultation the person who is seeking advice should be better able to function within the role of his particular job setting. The purpose is to help him carry out his teaching, policing, probation or other role more satisfactorily—not try to make of him a sort of "junior psychiatrist" or other mental health expert. Through this kind of help to community caretakers, a significant number of troubled or needy persons who are being dealt with by the caretakers are kept from becoming materialized psychiatric casualties who must enter the direct service treatment facilities of community mental health programs.

Community programs also traditionally include provision for psychiatric consultations to physicians concerning the emotional problems of their patients. Physicians, both general practitioners and specialists, are at present coping with the major

burden of mental illness in the community. Often with help from psychiatric consultation, general practitioners can be encouraged to continue in the demanding and frustrating care of patients with chronic psychiatric illness. Often for such patients the general practitioner is the most appropriate source of help. Current planning of community mental health centers emphasizes increased direct participation by physicians from general practice.

To provide the variety of direct and indirect service approaches described to this point, many pertinent elements in a community must be drawn together in a shared program. This will involve the integration of existing hospital and clinic services, government agencies, public health and private approaches into a coordinated operation consistent with the goals of the program and the resources of the community.

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# The Diarrhea of Travelers

## Incidence in Foreign Students in the United States

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■ *To ascertain whether foreign visitors to the United States experience the diarrhea of travelers, 215 foreign students matriculating at the University of California, Los Angeles, were interviewed. The attack rate of diarrhea was 14.0 per cent during the first month after arrival in the United States. In a comparison group of 238 U.S. students, the attack rate of diarrhea in one month was 8.4 per cent. The difference in attack rate was not statistically significant.*

*The diarrheal episodes reported by the foreign students were less abrupt in onset, less severe and of longer duration than the usual diarrhea of travelers. The typical severe explosive diarrhea of short duration usually described as "diarrhea of travelers" was not encountered among the foreign students in this study.*

*The occurrence of diarrhea was not associated with the age, sex or race of the students, with the location of eating places, with the geographic area from which the foreign students came or with any characteristics of the trip to the United States. In the group of U.S. students there was an increased incidence of diarrhea among students who came from outside California to Los Angeles.*

THE "DIARRHEA OF TRAVELERS" is often considered a disease of Americans who travel abroad, but its occurrence among travelers from other countries has been described.<sup>1,2,4,10</sup> Reports that diarrhea occurs in Mexicans traveling to California and in British visitors to New York City<sup>10</sup> indicate that travelers to the United States are not spared.

The cause of the diarrhea of travelers remains obscure. Studies by Kean and coworkers<sup>5-9,11,12</sup> failed to identify intestinal protozoa, viruses or species of *Salmonella* or *Shigella*. Widely accepted by travelers is the belief that diarrhea is related to ingestion of contaminated food or water exposed to less favorable sanitary conditions than in the United States.

If there is a significant incidence of diarrhea in visitors to the United States from abroad, this

would suggest factors other than poor sanitation as a cause of the disease. Other causal factors common to travelers could be postulated.

The present study was designed to test the hypothesis that diarrhea of travelers occurs in foreign citizens visiting the United States and to ascertain possible association with a variety of environmental and individual attributes.

### Method

A random sample of foreign students matriculating at the University of California, Los Angeles, was taken for study. For comparison a group of newly enrolled freshman students from within the United States was also taken at random. Both groups of students were interviewed during the routine entrance physical examinations in September 1964. Repeat interviews were obtained three to four weeks later from foreign students who had been in this country less than one month at the time of the initial interview.

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The questionnaires for the study group and the comparison group were similar. Questions were asked concerning the characteristics of the town or country where the student lived before coming to Los Angeles, previous and present eating and living arrangements, past history of gastrointestinal diseases, regularity of bowel movements, food intolerance, changes in bowel movements and other symptoms since arrival in Los Angeles. Questions pertaining specifically to details of the trip to the United States were asked of foreign students only. Although foreign students must be able to speak and to understand English before being admitted to the university, the degree of their understanding varies. Therefore, translations of some of the questions were available in Spanish, French, German and Chinese.

## Results

Initial interviews were obtained from 215 foreign students and 238 U.S. students. Fifty-seven foreign students were reinterviewed and another 12 who met the criterion for reinterview could not be found for repeat interviews.

While both the foreign and domestic students were entering UCLA for the first time, the demographic characteristics of the two groups were dissimilar. Of the 215 foreign students, 149 (69 per cent) were male; 119 (50 per cent) of the U.S. students were male. The mean age of the foreign students was 26 years, of the U.S. students 18 years. The foreign student group was composed of 46 per cent white, 48 per cent Oriental and 6 per cent Negro students; the United States group was composed of 95 per cent white, 3 per cent Oriental and 2 per cent Negro students.

## Attack Rates

For this study diarrhea was defined as any increase in frequency or looseness of bowel movements occurring within the period covered by this study, which is defined as the first month after arrival in the United States for foreign students and the month preceding the interview for U.S. students. Using these criteria, 30 (14 per cent) foreign students and 20 (8.4 per cent) U.S. students had diarrhea during the period. Twenty-five foreign students could state a date of onset. The mean onset time for this group was 3.8 days after arrival in this country, with 23 of the 25 cases occurring within the first week after arrival. When grouped in relation to the day classes started at

the university, there was no clustering of onset times among either foreign students or U.S. students.

The sex, age and race of the students with diarrhea did not differ significantly from those without diarrhea in either group of students. Data on the characteristics of illness in the two groups of students are given in Table 1.

## Medical History

Seventy-three foreign students (34 per cent) gave a past history of diarrhea or dysentery. Of these, 16 (22 per cent) had diarrhea during the first month after arrival in the United States. The attack rate among 142 foreign students who gave no past history of diarrhea or dysentery was 10 per cent, a significant difference ( $p=0.05$ ).

Among U.S. students, 163 (69 per cent) gave a history of diarrhea or dysentery; 11 per cent of these had had diarrhea during the month preceding interview. This attack rate was significantly different from the attack rate of 3 per cent in U.S. students with no past history of diarrhea or dysentery ( $p=0.05$ ).

## Travel History (Foreign Students)

The incidence of diarrhea was not associated with any of the following characteristics of the trip to the United States: duration of trip, mode of transportation or length of time spent in stops during the trip. Forty foreign students (19 per cent) had made previous visits to the United States. Their diarrhea attack rate was not significantly different from the attack rate among students who were visiting the United States for the first time.

The reported incidence of diarrhea in relation

TABLE 1.—*Clinical Characteristics of Diarrhea in Foreign and U.S. Students, University of California, Los Angeles, September 1964*

	Among 30 Foreign Students		Among 20 U. S. Students	
Duration of diarrhea (days).....1 to 28 (mean 8.8)			1 to 21 (mean 4.5)	
	Number	Per Cent	Number	Per Cent
Students:				
Restricting activities .....	3	10	1	5
Seeking treatment .....	5	17	2	10
Reporting associated symptoms:				
Abdominal pain .....	5	17	6	30
Nausea .....	4	13	1	5
Vomiting .....	1	3	0	...
Fever or chills.....	2	7	1	5

TABLE 2.—Length of Time in the United States and Attack Rate of Diarrhea Among 215 Foreign Students at University of California, Los Angeles, September 1964

Length of time in United States	Number of Students	Number with Diarrhea in First Month After Arrival	Attack Rate (Per Cent)
Less than 1 month.....	96	21	22
1 to 6 months.....	52	7	14
More than 6 months.....	67	2	3

to the length of time the foreign student had been in the United States is presented in Table 2.

The differences in attack rates are significant at  $p=0.01$ . However, the information on incidence of diarrhea was based on recall of an event occurring in the first month after arrival, and it seems probable that the students who had arrived most recently would recall more readily an episode of diarrhea than would those who had been in the United States several months.

#### Eating Arrangements

Both groups of students were asked what kind of food they were eating and where most meals were consumed. The responses to these questions are summarized in Table 3. Nineteen per cent of

foreign students were eating mainly foreign food (or food typical of home country). The incidence of diarrhea was not significantly related to type of food consumed or to the location of eating places.

#### Environmental Factors

Several characteristics of the communities from which the students came were examined. Population, urban vs. rural, and rainfall were not significant factors. Among the 35 foreign students who came from areas where it was cool-to-cold in July-August, 9 (26 per cent) had diarrhea; among the 179 who came from areas where it was warm-to-hot in July-August, as it is in Los Angeles, 21 (12 per cent) had diarrhea. This difference was significant at  $p=0.05$ .

The 52 countries represented by the foreign students in the study are grouped by geographic area in Table 4. There was no extraordinary incidence of diarrhea among students from any specific country or group of countries.

The locations from which the U.S. students came to the university were grouped as: (1) within Los Angeles or Orange Counties, (2) within California, excluding Los Angeles and Orange Counties, or (3) within the United States, exclud-

TABLE 3.—Location and Type of Food Consumption and Diarrhea Attack Rate Among Foreign and U.S. Students, University of California, Los Angeles, September 1964

	Foreign			U. S.		
	Number of Students	(Per Cent)	Attack Rate (Per Cent)	Number of Students	(Per Cent)	Attack Rate (Per Cent)
Predominant type of food eaten:						
American .....	174	81	15	232	97	15
Foreign .....	41	19	10	6	3	0
Location of most meals:						
House or apartment.....	152	71	15	128	54	7
Restaurant or dormitory.....	62	29	11	108	46	11
Not stated .....	1	....	....	2	....	....

TABLE 4.—Geographic Area of Origin and Attack Rate of Diarrhea in a Sample of Foreign Students, University of California, Los Angeles, September 1964

Geographic Area	Number of Students	Per Cent of Students	Number with Diarrhea	Attack Rate (Per Cent)
Asia .....	107	50	14	13
China (Taiwan, Hong Kong).....	36	17	3	8
Japan .....	32	15	6	19
India and Pakistan.....	9	4	1	11
Other Asian countries.....	30	14	4	13
Europe .....	34	16	5	15
Central and South America.....	32	15	7	22
Middle East .....	25	11	2	8
Africa .....	10	5	1	10
Other .....	7	3	1	14
	215	100	30	



TABLE 5.—*Geographic Area of Origin and Diarrhea Attack Rate in a Sample of Freshman U.S. Students, University of California, Los Angeles, September 1964*

Geographic Area	Number of Students	Number with Diarrhea	Attack Rate (Per Cent)
Los Angeles and Orange Counties.....	189	13	7
California, excluding Los Angeles—Orange Counties	33	3	9
United States, excluding California.....	16	4	25

ing California. The number of students and the incidence of diarrhea within each category are given in Table 5.

The differences in attack rates shown in Table 5 are significant ( $p=0.05$ ). Los Angeles and Orange Counties include all the cities and suburban areas which are near enough to the university to allow students to commute or to remain in close contact with their families, friends and home environment. Students from the remainder of California and the United States must make major shifts in living arrangements in order to attend UCLA.

Cause

Students reporting diarrhea were asked to state what they believed caused it. The answers are presented in Table 6. Foreign students more often attributed the diarrhea to ingestion of food or beverage while the U.S. students named some factor associated with the tensions and changes of entering the university.

Discussion

The attack rate for diarrhea of travelers ranges from 33 to 67 per cent in reported studies.<sup>2-4,9</sup> In a comparison group of travelers returning from Hawaii to Los Angeles, the attack rate was 7.6 per cent.<sup>6</sup> In several of the reported studies the period of time over which the attack rate is meas-

TABLE 6.—*Suspected Causes of Diarrhea as Reported by Foreign and U.S. Students, University of California, Los Angeles, September 1964*

Suspected causal factor reported	Number of Students	
	Foreign	United States
Water .....	2	1
Milk .....	4	0
Food .....	13	3
Travel .....	2	0
Change in routine.....	3	2
Nerves or excitement.....	1	6
Other .....	0	2
No opinion .....	5	6

ured is not given. In this study the incidence of diarrhea during a period of one month was 14 per cent in the foreign students and 8.4 per cent among the U.S. students in Los Angeles.

The clinical characteristics of the diarrheal episodes reported in this study differ from the usual syndrome of diarrhea of travelers among Americans traveling abroad. The latter is characterized by abrupt onset of loose or watery stools, accompanied by generalized abdominal pain and cramps, fever and nausea. Usually the patient is confined to his room for one or two days, after which he recovers rapidly and completely. The cases of diarrhea in the present report were generally less abrupt in onset, less severe and of longer duration, with few other symptoms. It is doubtful, therefore, that these cases represent the diarrhea of travelers as described in studies by Kean and others.

Questioning of foreign students regarding normal bowel habits and changes in frequency and consistency of stools was very difficult. A few students did not understand any of the terms used by the interviewers, and some of the others were hesitant to discuss the subject. These students were grouped with those not reporting diarrhea. The higher reported attack rate among foreign students who gave a past history of diarrhea or dysentery may be a reflection of better understanding of the terminology by these students.

The attack rate was 22 per cent among students who had been in the United States less than one month. This figure probably represents a closer approximation of the actual incidence. The lack of good recall by students here for a longer period may have lowered the overall reported attack rate.

Haneveld<sup>2</sup> studied the occurrence of diarrhea among the members of the United Nations Mission to Lebanon in 1958 and reported a difference in incidence in relation to the geographic area of origin of the members. A significantly higher incidence occurred among persons coming from Europe and North America than among those from Asia and South America. Haneveld also found a higher incidence of diarrhea among officers than among non-commissioned personnel in Lebanon. He suggested that there might be greater immunity among those persons with previous exposure to intestinal infection, as represented by non-commissioned personnel and by representatives from countries where sanitary facilities are insufficient. This theory presupposes that the diarrhea of travelers is usually due to intestinal infection. In the

present study there was an increased incidence of diarrhea in foreign students who came from areas where the July-August temperature was different from that in Los Angeles. Otherwise, there was no association between incidence of diarrhea and geographical origin of the foreign students.

In the comparison group of U.S. students the incidence of diarrhea was significantly higher in students who came from outside California to attend the university. Forty per cent of the U.S. students with diarrhea suggested "nerves," excitement or change of routine as a possible cause. Perhaps that was a correct assessment. Students who traveled from a farther distance may have been subject to more emotional disturbance.

The diarrhea which occurred in foreign students may have the same cause, for they were faced with the new experience of entering the university.

The question of whether the "diarrhea of travelers" does occur in foreign visitors to the United States has not been answered by this study; the 14 per cent diarrhea attack rate among foreign students was not significantly different from the 8.4 per cent rate among the comparison group. A prospective study in which foreigners are studied from the time of arrival in this country would be a better method of obtaining accurate data.

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# Antinuclear Antibodies and Nuclear Antigens

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■ *The lupus erythematosus (LE) cell factor is one of a variety of heterogeneous antibodies directed against many nuclear antigens. These antinuclear antibodies are found in a wide variety of clinical disorders. As detected by immunofluorescence techniques, they are so frequently found in association with systemic lupus erythematosus that their absence essentially excludes that diagnosis.*

*It is suggested that in certain situations other than systemic lupus, antinuclear antibodies may be the result of some inflammatory and destructive processes. Antinuclear antibodies may be detected in certain lower animals frequently in association with disease. In lower animals, immunization with nuclear antigens appropriately complexed\* to protein carriers consistently results in the induction of antinuclear antibodies. In both man and animals, antinuclear antibodies are often detected without associated disease. Furthermore, antinuclear antibodies are not injurious to intact tissue culture cells. Nonetheless, antigen-antibody complexes consisting of nuclear antigens and antinuclear antibodies may contribute to the propagation of certain diseases, particularly lupus nephritis.*

*The use of antinuclear antibodies as immunochemical tools holds great promise for the better understanding of such nuclear antigens as are found in viruses and in the nuclei of certain malignant cells.*

THE LUPUS ERYTHEMATOSUS (LE) cell phenomenon, discovered in 1948 by Hargraves, Richmond and Morton,<sup>16</sup> was the first demonstration of the reaction between antinuclear antibodies and nuclear antigens. A serum factor (the LE cell factor) was later shown to be essential for the production of the LE cell phenomenon. The LE cell factor was

found to be a gammaglobulin and is considered to be an antibody to nucleoprotein. The complex of antigen and antibody, nucleoprotein and the LE cell factor, is phagocytized by polymorphonuclear leukocytes to produce the characteristic LE cell<sup>30</sup> (Figure 1). Serum complement components, although not essential for the production of LE cells, are consumed in this reaction. A source of free nuclei, that is, nucleoprotein (antigen), the LE cell factor (antibody), and active leukocytes for phagocytosis are necessary for the production of LE cells.

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\*The term *complexed* is used here to describe the combination of nuclear material and some serum protein. This combination may be achieved by chemical covalent linkage, electrostatic combination, or by antigen-antibody combination.

Techniques involving different methods for traumatizing peripheral blood cells to obtain free nuclei were all shown to be effective in producing the LE cell phenomenon, although some methods resulted in a higher percentage of positive tests than did others.<sup>38</sup> Heparin was shown to inhibit the formation of LE cells, and this observation prompted other investigators to use heparin as a form of therapy in systemic lupus erythematosus,<sup>17</sup> where LE cells are particularly common. Similarly, chloroquin was found to inhibit LE cell formation.

The LE cell phenomenon has proved to be of great clinical diagnostic value, since relatively asymptomatic cases of systemic lupus erythematosus can be detected by its use. However, the LE cell phenomenon was also observed in conditions other than systemic lupus erythematosus. Among them were severe cases of rheumatoid arthritis, serum sickness, drug reactions and other collagen-vascular diseases. The LE cell factor was shown to be only one of many antinuclear antibodies present in the blood of patients with those conditions. Antinuclear antibodies were frequently detected by immunofluorescence techniques in cases of collagen-vascular disease where the LE cell tests were negative.<sup>6,19</sup> Most laboratories reported positive immunofluorescence tests for antinuclear antibodies in every case where the LE cell test was positive. Since the LE cell factor can also be detected by immunofluorescence techniques, the positive correlation between LE cell tests and immunofluorescence tests is easily understood.

Other antinuclear antibodies that are incapable of producing the LE cell phenomenon in even high concentrations are detected by immunofluores-

cence tests, which explains the positive antinuclear antibody tests in certain cases of collagen-vascular disease when the LE cell test is negative. Because of the almost universal association of antinuclear antibodies with systemic lupus erythematosus, a negative immunofluorescence test has been used to exclude this diagnosis.<sup>6,19</sup>

In addition to the antibody to nucleoprotein, the LE cell factor, there were found antinuclear antibodies to DNA (desoxyribonucleic acid), histone, phosphate extractable protein constituent of the nucleus, RNA (ribonucleic acid) polynucleotides, purines and pyrimidines. Antibodies to these antigens were detected in all the classical tests for antibodies including precipitation, complement fixation, agglutination, and passive cutaneous anaphylaxis (previously reviewed by Barnett and co-workers<sup>6</sup>). Stollar and Levine obtained much information regarding the specificity of anti-DNA (desoxyribonucleic acid) antibodies by the use of quantitative complement fixation techniques. Since the reaction with lupus serum and single strand DNA could be inhibited by polynucleotides<sup>33</sup> and purines,<sup>34</sup> many anti-DNA antibodies in lupus sera are directed against purines. Theophylline and theobromine were more active inhibitors than adenine, suggesting that the antibody to DNA might be the result of an immunization with a foreign purine, such as theophylline acting as an hapten, inducing antibody capable of cross-reacting with nucleic acid bases. They also found that chloroquin inhibited the complement-fixing reaction by binding to the nucleic acid bases of DNA.

Recently we studied an interesting patient with systemic lupus erythematosus who had anaphylactoid reactions to meralluride injection (Mercurydrin®). It is possible that the mechanisms of the patient's reactions depended on the reaction of theophylline in Mercurydrin® with the patient's anti-DNA antibody.

As with other antibodies against foreign antigens, antinuclear antibodies were shown to be immunoglobulins. They were heterogeneous in that they were demonstrated in three known immunoglobulin classes— $\gamma$ G,  $\gamma$ A, and  $\gamma$ M.<sup>5</sup> They were shown to have light polypeptide chains of both  $\kappa$  and  $\lambda$  type.<sup>3</sup> This heterogeneity of antinuclear antibodies was demonstrated using rabbit antisera specific for human  $\gamma$ G,  $\gamma$ A,  $\gamma$ M heavy polypeptide chains, as well as antisera specific for  $\kappa$  and  $\lambda$  light polypeptide chains (Figure 2).

The technique of demonstration is as follows:

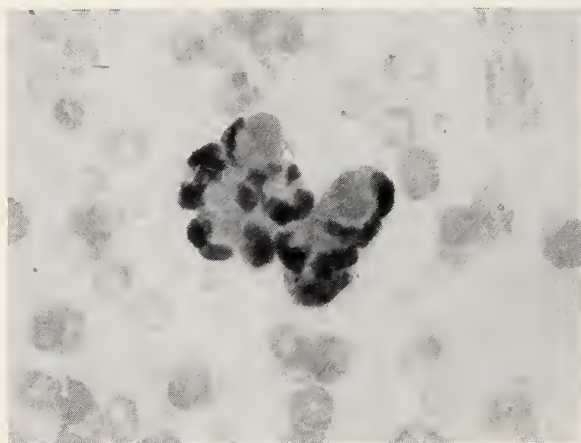


Figure 1.—Photomicrograph of a positive LE cell preparation stained with Wright's stain. Note the homogeneous pattern of the phagocytized nuclear material ( $\times 400$ ).



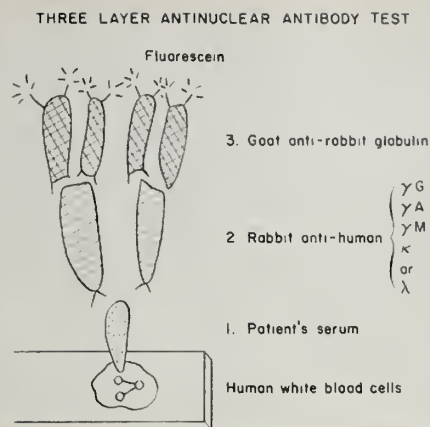


Figure 2.—Technique for three-layer antinuclear antibody test utilizing human leukocyte nuclei as source of antigen and rabbit antisera to specific antigenic determinants of human immunoglobulins.

Peripheral blood leukocytes in normal peripheral blood smears dried on glass slides are used as a source of nuclear antigens. These slides are then fixed in ethanol and an aliquot of the patient's serum is layered on the slide and allowed to incubate for 30 minutes. The next step is to wash the slides in buffered saline solution to remove the non-antibody proteins, after which a rabbit-anti-serum specific for  $\gamma G$ , or one of the other human immunoglobulins, is layered on the slide. The slide is allowed to incubate for 30 minutes and then again is washed in buffered saline solution. Thereafter, a fluorescein-conjugated goat antiserum to rabbit gammaglobulin is layered on the slide, which again is incubated for 30 minutes and washed. The preparations are mounted under glass coverslips and viewed through a dark field microscope with an appropriate ultraviolet light source.

This three-layered indirect immunofluorescence technique has the advantage of increased sensitivity, and it obviates the necessity of preparing fluorescein conjugates of highly purified rabbit anti-human H and L chains which are available only in small quantities. By use of this three-layered immunofluorescence technique to study chromatographically and ultracentrifugally separated fractions of human sera, it was found that antinuclear antibodies of the  $\gamma G$  immunoglobulin class were approximately 7S (160,000 molecular weight) in sedimentation rate and were eluted from di-ethylamino-ethyl (DEAE) cellulose columns with other  $\gamma G$  immunoglobulins.<sup>5</sup> The  $\gamma G$  antinuclear antibodies were resistant to sulfhydryl compounds.  $\gamma A$  antinuclear antibodies were very

heterogeneous in their sedimentation characteristics and showed varying sensitivity to inactivation by sulfhydryl compounds. A similar situation was also found with antinuclear antibodies having H chains of  $\gamma M^{31}$  immunoglobulin class in that, although the majority were 19S (1,000,000 molecular weight) and inactivated by sulfhydryl compounds, there were some that were more slowly sedimenting and resistant to inactivation by sulfhydryl compounds.

The sera of patients with systemic lupus tended to have high titers of antinuclear antibodies in the  $\gamma G$  class, while titers of antinuclear antibodies in the sera of rheumatoid arthritis patients were lower in the  $\gamma G$  class, but high in the  $\gamma M$  class of immunoglobulins. Data on children and adults with rheumatoid arthritis suggest that antinuclear antibodies appeared during the course of rheumatoid arthritis and were not present with the onset of the disease.<sup>6</sup> The  $\gamma M$  antinuclear antibodies were the first to appear and were followed later by the appearance of  $\gamma G$  antinuclear antibodies. The time sequence of antinuclear antibody production was similar to that demonstrated for other antibodies following immunization with foreign antigens. On this basis, it was suggested that in rheumatoid arthritis the antinuclear antibodies are produced as a result of immunization by the products of the inflammatory (arthritic) process.

In systemic lupus erythematosus, in the hydra-lazine syndrome, in lupoid hepatitis and in Sjogren's syndrome, antinuclear antibodies of all three immunoglobulin class were present in high titer at the time of first diagnosis.<sup>2</sup> In this situation, it is possible that if the antinuclear antibodies are a result of an immunization process, the process has been going on for a considerable time before diagnosis. This is in part supported by the observation of biologically false positive Wassermann tests long before the appearance of symptomatic lupus erythematosus.<sup>18</sup> The detection of antinuclear antibodies in all three immunoglobulin classes (their heterogeneity) makes it particularly unlikely that these autoantibodies are produced by a single abnormal clone of cells by some process of mutation.

Antinuclear antibodies as well as positive LE cell tests have been found in a variety of collagen-vascular diseases (cited in <sup>6</sup>). Differing percentages of positive tests have been found in these disorders in different laboratories. These differences may be explained by differences in the nuclear

substrate, the specificity and the quantity of antibody to human gammaglobulin, the degree of fluorescein conjugation of the antibody,<sup>20</sup> and the brightness of the ultraviolet light source used for the microscope, as well as by differences in patient selection. Nonetheless, similar serologic abnormalities in these disorders suggest some common pathogenetic pathways. This does not imply that the primary etiologic factors are identical in these clinically divergent disorders. We may have a situation analogous to the detection of positive Wassermann antibodies in such clinically divergent infectious diseases as syphilis, leprosy and infectious mononucleosis. Indeed, antinuclear antibodies as well as rheumatoid factors have been found in a large proportion of patients with leprosy<sup>24</sup> and syphilis, and have been reported following infectious mononucleosis. This may suggest that as sequelae of certain infectious diseases there is sufficient tissue destruction and release of nuclear antigens to elicit antinuclear antibodies, as well as sufficient release of other antigens to elicit the Wassermann antibody and the rheumatoid factor.

Detection of small amounts of antinuclear antibodies by highly sensitive tests in normal persons<sup>21</sup> and the increased incidence of these antibodies in aged populations<sup>11</sup> is also compatible with the hypothesis that in some cases the aging process, with its attendant chronic tissue destruction, is itself sufficient for the induction of auto-antibodies.

Earlier reports suggested that antinuclear antibodies were not specific for the nuclei of any one species or of any one organ. Other data have suggested that in rheumatoid arthritis, antinuclear antibodies are best detected on peripheral leukocyte nuclei and have a relative specificity for leukocyte nuclei.<sup>6</sup> Antibodies to desoxyribonucleic acid, although found in other collagen-vascular diseases, are certainly more common in systemic lupus erythematosus.<sup>12</sup> By the immunofluorescence tests, it has been suggested that a shaggy fluorescence pattern is indicative of antibody to DNA and is specific for the diagnosis of systemic lupus erythematosus<sup>12</sup> (Figure 3). Although this is frequently the case, there are many sera with a shaggy pattern in which no antibody to DNA is detectable by other techniques and where the clinical diagnosis is other than systemic lupus erythematosus (Figure 4). The bright solid immunofluorescent pattern (Figure 5) has been suggested to be indicative of antibody to nucleoprotein, the speckled

pattern (Figure 6) for antibody to the phosphate-saline extractable protein antigen of the nucleus, and a nucleolar pattern for antibody to a protein associated with RNA (cited in reference 6). In addition, a peri-nuclear pattern<sup>27</sup> has also been described as well as bright cytoplasmic fluorescence (Figure 6).

Antinuclear antibodies have been described in spontaneously occurring systemic lupus erythematosus of dogs, many strains of mice and even chickens. They have been induced in rabbits by immunization with single strand-DNA complexed to bovine serum albumin. Anti-DNA antibodies have also been detected in rabbits following immunization with whole human serum in Freund's adjuvant.<sup>7</sup> This observation suggests that there are nuclear antigens in human serum so complexed with human serum proteins that when injected with Freund's adjuvant into rabbits, antinuclear antibodies are produced. Similarly, antibodies to DNA have been induced by immunization with protein conjugates of purines, pyrimidines and polynucleotides (cited in reference 7). Since in both man and animal, antinuclear antibodies are frequently detected in the absence of clinical disease, it seems unlikely that the antibodies themselves cause disease. This conclusion is supported by the failure to induce disease by transfusion of blood from patients with lupus erythematosus,<sup>23</sup> although LE cells and antinuclear antibodies may appear in the blood of the recipient. The usual benign course of infants born to mothers with systemic lupus erythematosus and the absence of cytotoxicity of lupus serum on cells grown in tissue culture<sup>37</sup>

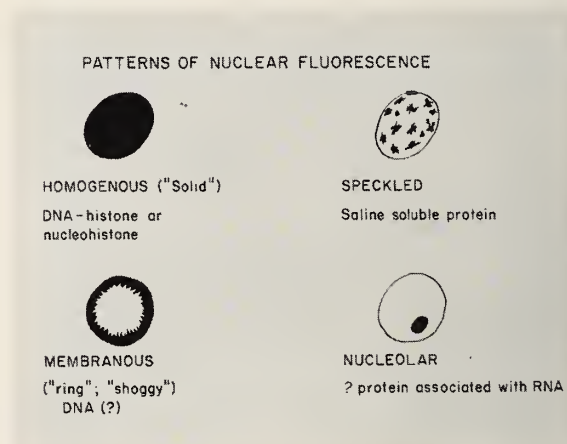


Figure 3.—Schematic representation of the patterns of nuclear fluorescence obtained with sera from patients with systemic lupus erythematosus, utilizing human leukocytes as a source of nuclear antigens.



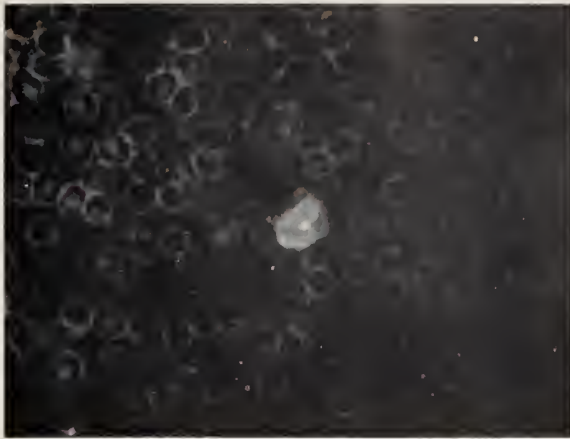


Figure 4.—Photomicrograph of an immunofluorescence test for antinuclear antibodies in the serum of a patient with rheumatoid arthritis. Note shaggy pattern ( $\times 250$ ).

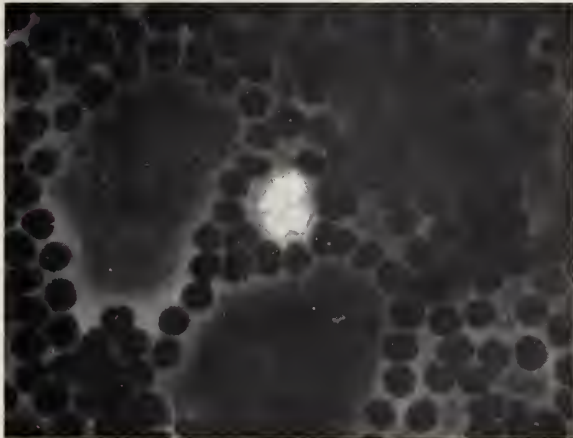


Figure 5.—Photomicrograph of an immunofluorescence test for antinuclear antibodies in the serum of a patient with lupus erythematosus. Note solid pattern. ( $\times 250$ ).

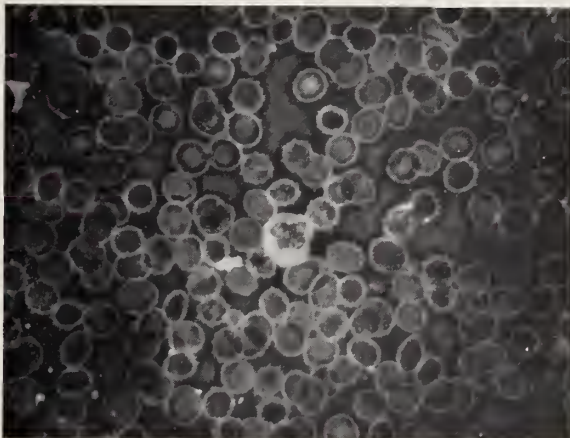


Figure 6.—Photomicrograph of an immunofluorescence test for antinuclear antibodies in the serum of a patient with lupus erythematosus. Note speckled nuclear pattern and cytoplasmic fluorescence ( $\times 250$ ).

further suggest that the antibodies by themselves are not injurious. Although antinuclear antibodies are not toxic to intact cells, they have been shown to inactivate viral DNA,<sup>10</sup> a situation where the DNA is inadequately protected by a protein coat. Therefore, antinuclear antibodies may have a toxic effect on the nuclei of cells where the protective cellular and nuclear membranes have already been injured by another primary disease process. Furthermore, nuclear material released from inflamed tissue may react with antinuclear antibodies, resulting in the formation of antigen-antibody complexes.

Complexes of antigens and antibodies have been incriminated in the production of vasculitis, nephritis and synovitis in experimental animals. There are certain observations which suggest that antinuclear antibodies may react with nuclear antigens *in vivo* and fix complement during the course of systemic lupus erythematosus. The depression of complement levels associated with the high titers of antinuclear antibodies in severe cases of systemic lupus erythematosus<sup>26</sup> is in accord with this hypothesis. Furthermore, immunoglobulins and complement components have been found bound to nuclei in the inflamed skin of patients with systemic lupus erythematosus,<sup>35</sup> and immunoglobulins and complement components have been detected in the glomerular lesions of lupus nephritis.<sup>22</sup> Freedman and Markowitz<sup>15</sup> suggested that the immunoglobulins in lupus glomeruli were antinuclear antibodies that were presumably complexed there with nuclear antigens and complement components.

High levels of circulating DNA have been demonstrated in occasional patients with systemic lupus erythematosus, as well as in other situations involving massive break-down of tissue.<sup>36</sup> The detection of such circulating antigens in a situation where antibody is available, further emphasizes the possibility that nuclear antigen-antibody complexes might have a pathogenic role in systemic lupus erythematosus. It should be considered, however, that the situation in the patient with lupus may only be quantitatively different from that in normal persons, since low levels of circulating DNA have been demonstrated in many of the latter.<sup>2</sup>

The increased level of circulating DNA in systemic lupus erythematosus is not likely the sole cause for the production of antinuclear antibodies.

This statement is based on the repeated failure to induce antinuclear antibodies in animals by repeated immunization with nuclear antigens alone. However, antinuclear antibodies, particularly anti-DNA antibodies, have been produced in experimental animals by immunization with DNA that is complexed or conjugated to carrier proteins. Is the large quantity of DNA present in lupus blood so complexed to serum proteins that it is auto-antigenic? Also to be considered is the role of serum nucleases in the scheme. Increased serum DNA may be the result of abnormal or increased synthesis of DNA, abnormal or increased destruction of nuclear material releasing DNA, abnormalities in nucleases resulting in inadequate removal of DNA, as well as abnormalities in serum binding of DNA so that the DNA or nuclear material is antigenic to the host.

These are only a few of the possibilities responsible for the production of antinuclear antibodies in human disease. Indeed the methods of antinuclear antibody induction may well be different in the various collagen-vascular diseases. In patients with rheumatoid arthritis it has been demonstrated on occasion that both rheumatoid factor and antinuclear antibodies may be detected in synovial fluid when none is detectable in the patients' serum.<sup>4</sup> These observations considered in the light of the detection of large numbers of antibody-producing plasma cells in the synovium, suggest that these auto-antibodies—that is, rheumatoid factor and antinuclear antibodies—are produced locally in the inflamed joints.

We have recently detected large amounts (greater than 100-fold increases) of DNA in synovial fluid as compared with the serum of patients with rheumatoid arthritis. This observation is in accord with those by Zvaifler and others (cited in reference 4) who detected Feulgen-positive material in cytoplasmic inclusions of rheumatoid synovial leukocytes. On the basis of this observation it has been suggested that the reaction between nuclear antigens and antibodies in synovial fluids may account for the depressed synovial fluid complement levels found in rheumatoid arthritis. This DNA may be the product of the rapid and extensive leukocyte turnover in the inflamed synovial fluid. It would then be possible for the nuclear materials to complex with the serum proteins present in high concentration in rheumatoid synovial fluid. The DNA-serum protein complex might immunize the individual locally so that antinuclear antibodies are

produced first in the synovial fluid, and later after continuous and severe inflammation and immunization, would be detectable in the patients' serum.

In addition to the importance of antinuclear antibodies and nuclear antigens in the pathogenesis of collagen-vascular diseases, antinuclear antibodies have proved to be valuable tools for the immunochemical characterization of desoxyribonucleic acid constituents. By use of immunofluorescence techniques, tissue culture cells infected with virus have been shown to contain cytoplasmic desoxyribonucleic acid and nucleoproteins.<sup>29</sup> The production of antibodies with a potential to discriminate between different sources of nuclear antigens including DNA may be of particular value for the study of tumor oncogenesis.<sup>9,25,28</sup> Although such reports have been received with optimism, there is sufficient precedence to believe that these techniques will prove inadequate for such differentiation.<sup>32,33,34</sup> It has recently been suggested that metastasis may be induced by circulating tumor DNA as well as by whole cells.<sup>8</sup> The immunochemical identification and quantitation of such abnormal DNA may be the extreme value for our understanding of oncogenesis. The influence of immunity to nuclear antigens on oncogenesis is receiving increasing attention.

Immunofluorescence techniques are being used to study nuclear antigens transformed by virus infection. If the viral genome induces antigenic changes in nuclear material during the process of oncogenesis,<sup>14</sup> we may consider the possibility that antinuclear antibodies in human disease are the manifestation of an immunologic response to nuclear material that has undergone some alteration by an intranuclear infectious process.

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#### GENERIC AND TRADE NAMES OF DRUGS

Meralluride injection—*Mercurydrin*.

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# CASE REPORTS

## Goodpasture's Syndrome

### Report of a Case with an Unusual Clinical Course

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THE SYNDROME of acute pulmonary alveolitis associated with glomerulonephritis, first described by Goodpasture,<sup>5</sup> is being more frequently recognized. Benoit and coworkers,<sup>1</sup> in a recent review considered the syndrome to be a distinct pathological entity. The disease appears to affect mainly Caucasian males under 30 years of age. Eight cases have been reported in females.<sup>1,2,4,12,13</sup> Only one occurrence has been described in a Negro male.<sup>1</sup> Goodpasture's syndrome is generally considered to be a fatal disease although documented survivals have occurred.<sup>4,10</sup>

Patients with this disease usually seek medical attention because of hemoptysis. A diffuse pulmonary infiltrate is usually present and most patients have a history of previous pulmonary or renal infection. Terminal massive hemoptysis along with azotemia and proteinuria usually occur.

The purpose of this report is to present a case of histologically documented Goodpasture's syndrome in which there were certain heretofore un-

reported clinical manifestations. This appears to be the first reported occurrence of this entity in a Negro female. The initial and only sign of illness was hemoptysis signifying an acute pulmonary disease. There was no history of symptoms indicating previous pulmonary or renal disease.

### Report of a Case

The patient, a 17-year-old Negro girl, was admitted to the Los Angeles County General Hospital on 3 January 1965 with complaint of a severe cough productive of blood-tinged sputum, which had been present for two days. She had been entirely well until the evening of the day of onset. Then fever and chills suddenly developed, with severe cough productive of a moderate amount of yellow blood-streaked sputum. By the day of admission she had substernal pain, described as aching, which occurred mainly while walking or with deep breathing or after severe coughing paroxysms. The chest pain was accompanied by dizziness and headache when she stood or walked. Two penicillin injections given by a physician before she entered the hospital had not relieved the symptoms. The patient then had been told that she was anemic and probably had severe pneumonia, and she was referred to this hospital.

The patient said that she had experienced loss of weight and weakness for three months. She also had noted a slight yellowing of the palms of her hands during the past three weeks. Three years previously she had been in close contact with a friend who once had had active tuberculosis and was being examined periodically by a Health Department physician. Chest roentgenograms and sputum cultures showed no recent active recurrence.

The patient had had no other serious illnesses or operations or injuries, she knew of no allergic sensitivity, and she had not had dysuria, hematuria, pyuria, nocturia or frequency. She smoked approximately 10 cigarettes a day. For four

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months she had been taking a quinine-type drug for premenstrual tension.

The patient was thin and well developed. The temperature was 38.6°C (101.4°F), and the pulse rate was 120 per minute and regular. Respirations were 40 per minute and regular. The blood pressure was 110/50 mm of mercury. The sclerae were clear, the conjunctivae pallid, the pupils equally reactive to light and accommodation and the fundi normal. No abnormalities were noted in the ears, nose and throat. The neck was supple and no venous distension was noted. A few shotty non-tender lymph nodes were palpable in the right posterior cervical and sub-mandibular areas. The thorax was symmetrical, with equal respiratory excursions bilaterally. Pronounced tachypnea was noted. Diaphragmatic excursions were shallow. There was slight dullness to percussion over both lung bases. Scattered inspiratory rales and rhonchi were present throughout both lung fields.

On examination of the heart the point of maximal impulse was located in the left fifth intercostal space at the mid-clavicular line. No heaves, thrills or friction rubs were noted. The apical rate was 120 per minute and regular. No murmurs were audible. The abdomen was scaphoid, bowel sounds were active and no abnormalities to percussion were noted. No masses or areas of tenderness were detected, and the liver and spleen were not palpable. The breasts were normal. Pelvic and rectal examinations were within normal limits. There was mild pallor of the palms of the hands. No peripheral edema, excoriations or other lesions of the skin were observed.



Figure 1.—X-ray showing diffuse bilateral infiltrate with a nodular appearance in the upper lung fields.

The patient was alert and walked without difficulty. The deep tendon reflexes were slightly hyperactive bilaterally. No pathologic reflexes were elicited.

A roentgenogram of the chest (Figure 1) showed a diffuse miliary infiltrate throughout both lung fields.

### Laboratory Data of Blood

The hemoglobin level was 5.2 gm per 100 ml and leukocytes numbered 17,000 per cu mm with 66 per cent polymorphonuclear leukocytes, 2 per cent band forms, 16 per cent lymphocytes, 9 per cent monocytes, 6 per cent eosinophiles and 1 per cent metamyelocytes. The specific gravity of the urine was 1.015, the pH 5.0, and there was a trace of protein and acetone<sup>o</sup> and a 1 plus reaction for sugar. The urinary sediment contained many leukocytes per high powered field without red cells or casts. The blood glucose was 110 mg and the blood urea nitrogen level 19 mg per 100 ml. The serum potassium concentration was 4.4 mEq, sodium 138 mEq and bicarbonate 18 mEq per liter. A smear of the sputum showed occasional Gram-positive and Gram-negative bacilli, type not identified. The intermediate purified protein derivative, histoplasmin and coccidioidin skin tests were all negative at 48 hours. Hemoglobin electrophoresis demonstrated SA hemoglobin. The total serum bilirubin concentration was 0.3 mg per 100 ml with a direct bilirubin content of 0.1 mg per 100 ml. The alkaline phosphatase level was 3.5 Bessey and Lowry units. The total serum iron level was 28 micrograms per 100 ml and iron-binding capacity 300 micrograms per 100 ml with a saturation of 9 per cent. Result of a direct Coombs test was negative. Three sputum concentrates for acid-fast bacilli were negative. Two specimens of sputum were negative for malignant cells.

### Hospital Course

The probability that the patient had acute pneumonitis was considered and she was given penicillin, 5,000,000 units intravenously daily for the next three days. However, her condition continued to deteriorate progressively. A review of the clinical course and the x-ray film of the chest suggested the possibility of acute miliary tuberculosis. Consequently, on the third hospital day, administration of streptomycin 1.0 gm, para-aminosalicylic acid 12 gm, and isoniazide 400 mg daily





Figure 2.—Section of left lung showing generalized intra-alveolar hemorrhage and blood-stained swollen hilar lymph nodes (Hematoxylin-eosin stain reduced by 75 per cent).

was begun. On the fifth hospital day a sputum culture grew *Streptococcus viridans* and *Neisseriae*.

The hemoglobin level had decreased to 2.8 gm per 100 ml and leukocytes numbered 17,400 with a differential cell count similar to that obtained on admission. Two nucleated red cells per 100 white cells were now noted on a blood smear. A roentgenogram of the chest showed no significant change in the diffuse infiltrate noted on the admission film. Due to the extensive loss of blood from hemoptysis the patient received 1,000 ml of whole blood. She continued to have profuse hemoptysis and on the sixth hospital day an episode of massive bleeding was followed by cardiac arrest. She died despite vigorous attempts at resuscitation.

### Autopsy

The post-mortem examination was performed 19 hours after death. The right and left lungs weighed 900 gm and 700 gm, respectively, and were similar in gross appearance. The pleural surfaces were smooth and dark red. The cut surfaces bulged and were uniformly dark red and

hemorrhagic; the parenchyma was non-aerated and there was pronounced increase in consistency. The tracheobronchial tree contained dark red, bloody fluid. The pulmonary arteries and veins were not abnormal in appearance. The hilar lymph nodes were soft, blood-stained and swollen.

Microscopically, the majority of the alveolar spaces were filled with blood, and some alveoli contained organized, eosinophilic, fibrinous exudates (Figure 2). Scattered aggregates of polymorphonuclear leukocytes and hemosiderin-laden macrophages were seen in both alveolar spaces and in the interalveolar septae (Figure 3). Some thickening of alveolar septae and proliferation of the alveolar lining cells was present. Focal hyaline membrane formation was also noted. Vasculitis was not observed, but the alveolar capillary basement membranes demonstrated sporadic, irregular splitting and fraying (Figure 4). Silver impregnation revealed proliferation of reticulum in some interalveolar septae. The Prussian blue reaction showed iron in macrophages but no iron impregnation in the lung parenchyma (Figure 5).

The right and left kidneys weighed 170 gm and 180 gm, respectively, and were similar in ap-

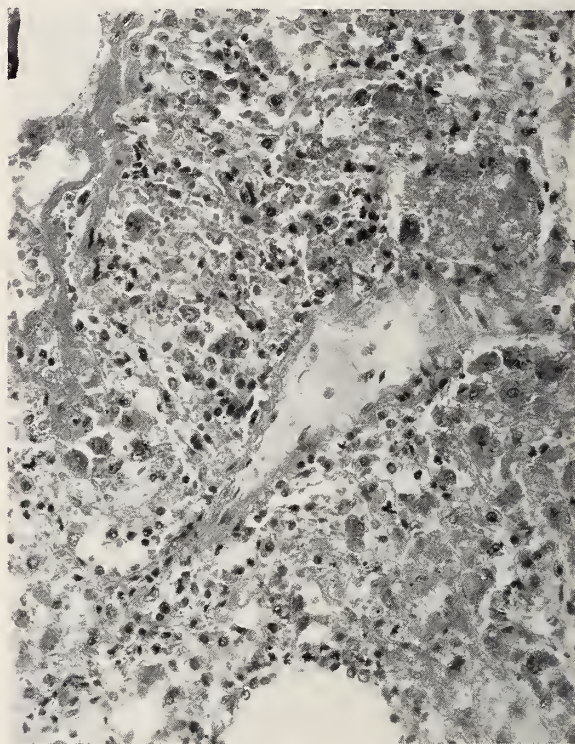


Figure 3.—Section of lung demonstrating hyaline membranes on some of the alveolar walls. Alveolar spaces are filled with extravasated blood, hemosiderin-laden macrophages and fibrinous exudates (Hematoxylin-eosin,  $\times 200$ ).



pearance. They were moderately enlarged and soft. The capsules stripped with ease, revealing a smooth surface. On section, the cortex was pale tan, was 1 cm thick and well demarcated from the dark red, bulging medulla. The pyramids, calyces and pelvis appeared normal.

Microscopically, the major lesion was glomerulitis, which did not involve all glomeruli. Approximately half the glomeruli were normal, while the remainder showed varying degrees of alteration. The earlier stage of the lesion (Figure 6) showed occlusion of the glomerular capillary loop by eosinophilic fibrinoid material and focal swelling of the epithelial cells. The intermediate stage of the lesion (Figure 7) showed proliferation of epithelial cells of the glomerulus, initially involving only a tuft, then a lobule, and finally the entire glomerulus. Fibrinoid necrosis of the glomerular tufts was also occasionally seen. The later stage of the lesion (Figure 8) showed progression of cellular proliferation to crescent formation, and even total obliteration of the glomerulus. No significant basement membrane thickening was

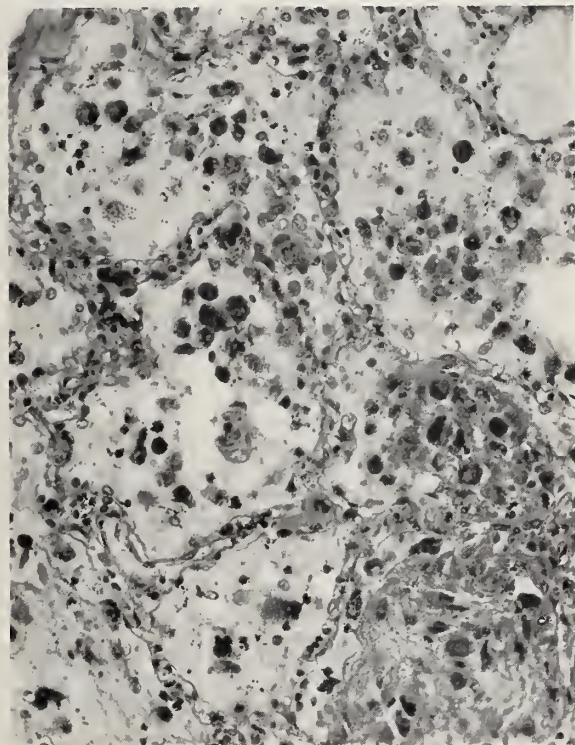


Figure 4.—Section of lung demonstrating scattered aggregates of polymorphonuclear leukocytes and hemosiderin-laden macrophages in both alveolar spaces and interalveolar septae. Sporadic irregular splitting and fraying of basement membrane are also seen (Periodic acid Scheff stain,  $\times 200$ ).

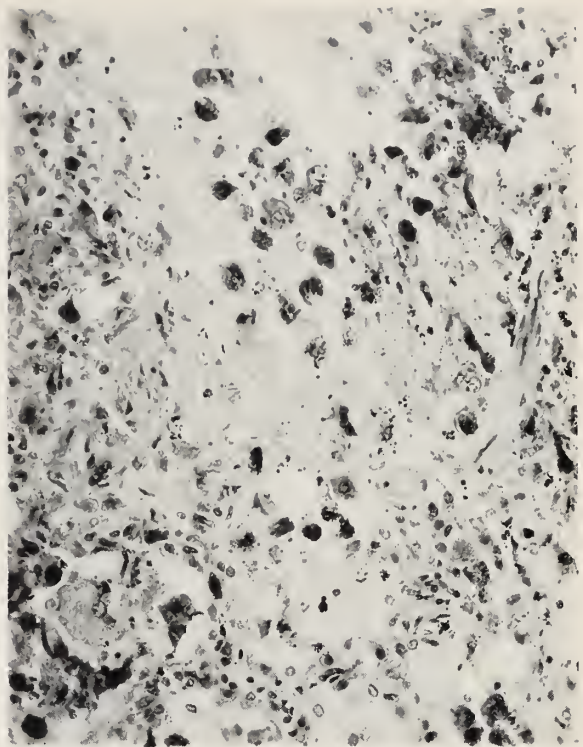


Figure 5.—Section of lung demonstrating absence of iron pigment impregnation in the lung parenchyma including elastic fibers of capillaries and interalveolar septi. Note: Iron pigment was seen only in the macrophages (Iron stain,  $\times 200$ ).

noted. There was no vasculitis. In the interstitial tissue there was occasional inflammatory cell infiltration around glomeruli. The tubules and vessels did not show significant changes. Culture of the lung specimen at autopsy revealed staphylococcus albus, coagulase negative; no acid-fast bacilli were isolated.

### Comment

The clinical, radiological and pathological features in the present case are similar to those reported in Goodpasture's syndrome.<sup>1,8,10,11</sup>

The absence of clinical evidence of renal involvement antemortem was probably due to the death of the patient before it developed. The patient died from suffocation which was secondary to massive intra-alveolar hemorrhage before full development of the syndrome.

The autopsy findings were those of the early stage of the natural history of the disease.

We do not think that this was a case of idiopathic pulmonary hemosiderosis, as has been suggested by McCall.<sup>7</sup> Idiopathic hemosiderosis seldom involves the kidney. Renal lesions were



present in only five of a total of 69 recorded cases of idiopathic pulmonary hemosiderosis reviewed by Heptinstall.<sup>6</sup> The lesions were mild and were considered to be either focal embolic nephritis or some other non-specific nephritides which might have been pre-existed. The kidney lesion in the present case was not only more extensive but also met all the histological criteria of Goodpasture's syndrome mentioned by Benoit.<sup>1</sup>

There is no single clear-cut histological criteria to be used in differentiating lung lesions of Goodpasture's syndrome from idiopathic pulmonary hemosiderosis. However, such findings as intra-alveolar fibrin deposition, fusiform swelling of alveolar septi, fraying and disruption of alveolar basement membrane are some of the features to be seen commonly in Goodpasture's syndrome, as was pointed out by Soergel and coworkers.<sup>14</sup> The lung lesion in the present case met all the histological criteria mentioned by them.

Idiopathic hemosiderosis is a disease of relatively long duration as compared with Goodpas-

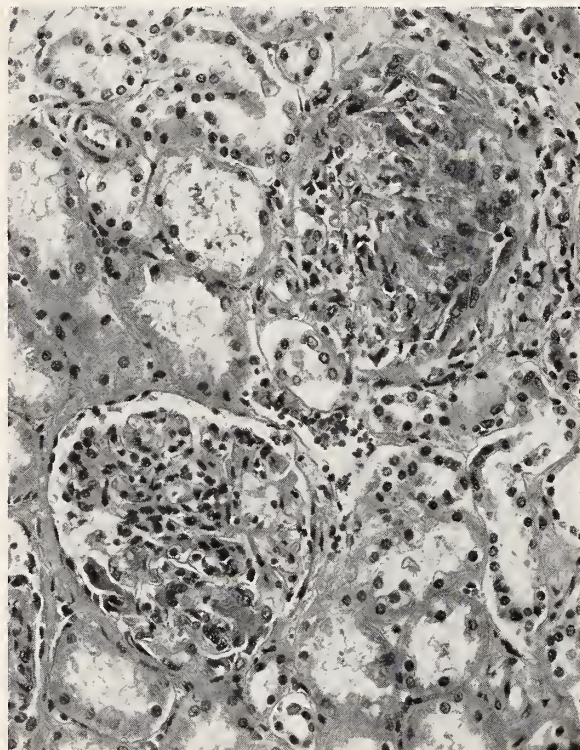


Figure 6.—Section of kidney demonstrating earlier and later stages of glomerulitis. The earlier lesion shows occlusion of glomerular capillary loop by eosinophilic fibrinoid material accompanied by focal swelling and proliferation of epithelial cells. The later lesion shows decided proliferation of glomerular epithelial cells and periglomerular inflammatory reaction (Hematoxylin-eosin,  $\times 200$ ).

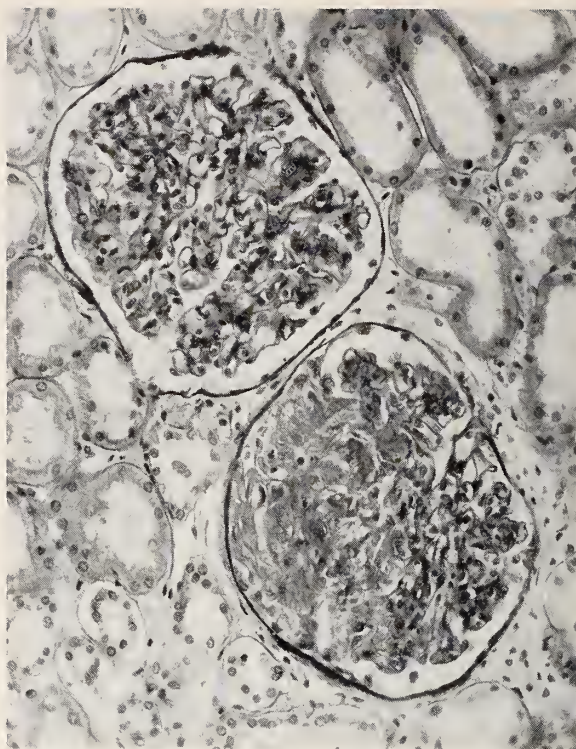


Figure 7.—Section of kidney demonstrating relatively intact glomerulus and intermediate stage of glomerulitis. The intermediate lesion shows a glomerular crescent formation by decidedly proliferated epithelial cells (Periodic acid Schiff stain,  $\times 200$ ).

ture's syndrome. Chronic intra-alveolar hemorrhage often produces extensive pulmonary fibrosis and iron impregnation in the elastic fibers of capillaries and interalveolar septi. Iron stain of the lung specimen in the present case failed to show such features.

The exact etiologic lineation of Goodpasture's syndrome is not known. However, it has been proposed that the syndrome represents a primary viral disease of the lung with secondary involvement of the kidney.<sup>4</sup> Autoimmune antilung antibody produced in animals has been shown to cross react with rat renal tissue, specifically with glomerular capillaries.<sup>9</sup> It is conceivable, as has been suggested by other investigators,<sup>3,10</sup> that lung tissue destroyed and altered by a viral agent might become antigenic and produce autoimmune antilung antibody which would cross react with one's own kidney to produce glomerulonephritis.

## Summary

A case of Goodpasture's syndrome in a 17-year-old Negro girl is described. She had had no antecedent illness of either the respiratory or renal



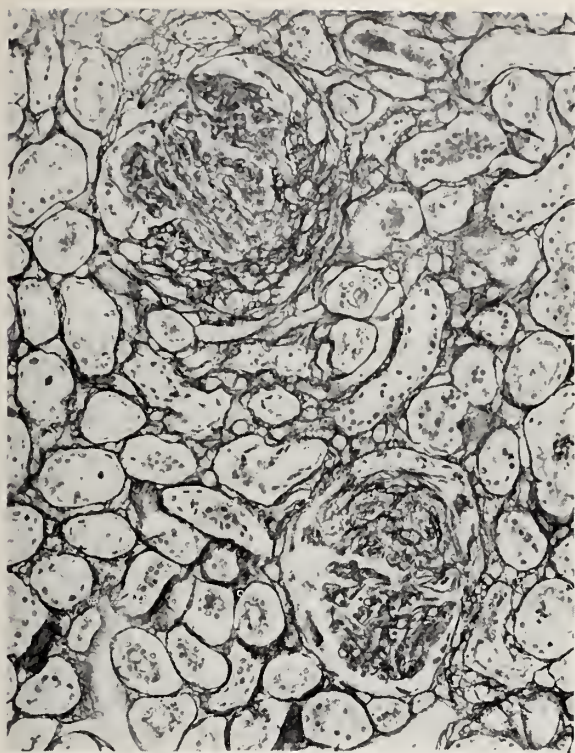


Figure 8.—Section of kidney demonstrating pronounced proliferation of reticulum fibers at the site of a glomerular crescent (Silver impregnation.  $\times 150$ ).

systems. The course of illness was very short—seven days. Autopsy findings were consistent with the early stages of the natural history of the disease.

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## Hemophilus Aphrophilus Endocarditis

### Successfully Treated With Ampicillin and Streptomycin

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THE FIRST KNOWN infection caused by *Hemophilus aphrophilus* was bacterial endocarditis in a 28-year-old woman who lived 165 days after admission to the hospital in 1938.<sup>13</sup> The name *Hemophilus aphrophilus* was chosen by Khairat<sup>13</sup> because of the hemophilic character of the organism, its dependence on hemin ( $x$  factor) and its enhanced growth in carbon dioxide. (Aphros from the Greek, meaning foam, refers to the carbon dioxide bubbles forming on wine vats during fermentation.) The organism does not require diphosphopyridine nucleotide ( $v$  factor) for growth. There have been fewer than 10 reported cases of bacterial endocarditis caused by this organism.\* In only one case, that reported by Quinn and co-workers,<sup>19</sup> was the patient treated with ampicillin.

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Submitted 11 January 1966.

\*Reference Nos. 12, 19, 21, 23, 26.



In the present case, the organism that grew on 12 blood cultures was identified as *Hemophilus aphrophilus* by the Department of Public Health Bacteriological Laboratories, State of California, and the U.S. Public Health Service, Communicable Disease Center, Atlanta, Georgia.

### Report of a Case

A 24-year-old Mexican man, a printer, was admitted to the White Memorial Hospital on 6 April 1965, with complaint of fever of 10 days' duration. He had not had recent dental work. He had had a heart murmur since age 16 and a history of probable rheumatic fever at age eight. Five years before admission, cardiac catheterization at Stanford University Medical Center established a diagnosis of mitral insufficiency. The patient had never had symptoms or signs of congestive heart failure. He had never received penicillin prophylaxis or digitalis.

On physical examination, the patient's oral temperature was 38.4°C (101.2°F). The pulse was regular at 108 per minute, the respiratory rate was 18 per minute and the blood pressure was 130/76 mm of mercury. The patient appeared well. The optic fundi were normal, and there were no dental caries, petechiae, splinter hemorrhages or clubbing. There was a moderate left ventricular heave with the point of maximum impulse palpable 2 cm lateral to the mid-clavicular line in the left 6th intercostal space. No thrill was palpated. A grade 4 (of 6) harsh, blowing, pansystolic murmur was heard at the apex and radiated toward the axilla. A faint diastolic rumble was heard at the apex with the patient in the left lateral decubitus position. The first heart sound at the apex was loud and the pulmonary second sound was accentuated. The lungs were clear. The liver was not palpable. The tip of the spleen was palpated beneath the left costal margin. All arterial pulses were normal.

The urine was clear and it did not contain protein, red cells or casts. The hemoglobin was 13.5 gm per 100 ml and the hematocrit 42 per cent. Leukocytes numbered 9,500 per cu mm with 37 per cent lymphocytes, 2 per cent monocytes, 1 per cent basophils and 55 per cent polynuclear and 5 per cent band neutrophils. The sedimentation rate (Westergren) was 68 mm in one hour. The two-hour post prandial blood sugar 128 mg, serum bilirubin 0.6 mg and the blood urea nitrogen 7 mg per 100 ml. Antistreptolysin O titer was 166 Todd units. A serological test for syphilis was nonreac-

tive. Serum sodium, potassium and carbon dioxide content were normal. Serum protein electrophoresis showed 4.0 gm of albumin and 4.3 gm of globulins per 100 ml, with elevated alpha 2 and gamma globulin fractions measuring 870 and 2,075 mg per 100 ml respectively. An electrocardiogram showed sinus tachycardia and occasional premature ventricular contractions. Tele-roentgenograms of the chest demonstrated mild left ventricular and left atrial enlargement.

In view of the persistent fever, splenomegaly, known valvular heart disease, elevated sedimentation rate and abnormal content of serum proteins, it was decided to treat the patient for bacterial endocarditis in spite of the fact that after four days' incubation there was no growth of organisms on six blood cultures drawn on admission. Six additional blood cultures were drawn and therapy was begun, consisting of a continuous intravenous infusion daily of 15,000,000 units of penicillin G, plus streptomycin, 1 gm daily, by intramuscular injection. On the sixth hospital day, colonies of small Gram-positive bacilli first appeared on all six of the blood cultures drawn on the day of admission, which had been incubated with 5 per cent carbon dioxide. The organism appeared to be of the *Hemophilus* species but not *H. influenza*.

By the eighth hospital day, there had been no clinical response to therapy. Since ampicillin has good activity in vitro against *H. influenza* and has been used successfully in the treatment of other *Hemophilus* infections,<sup>10,16,20,22</sup> use of this antibiotic was started on the eighth hospital day and penicillin G was discontinued. Ampicillin (Polycillin-N®), 2 gm diluted in 50 ml of water, was given intravenously by rapid infusion every four hours, the 24-hour dose being 12 gm. In addition, the streptomycin was increased to 2 gm intramuscularly each day. The patient did not have undesirable side effects. Ampicillin was continued at 12 gm daily for 29 days and streptomycin was given concurrently in a dose of 2 gm daily for 24 days. On the sixth day of ampicillin therapy, the temperature became normal. No splinter hemorrhages, petechiae or Osler's nodes were noted during the patient's 38 days in hospital. The character of the cardiac murmur did not change. The spleen, which was palpable 4 cm below the left costal margin on the 14th hospital day, was not palpable at the time of discharge. The sedimentation rate (Westergren) was 68 mm in one hour on admission, rose to a maximum of 109 mm on the eighth



hospital day, dropped to 26 mm at the time of discharge, and one month after discharge was 5 mm in one hour. Serial blood cell counts, urinalysis, and blood urea nitrogen determinations remained within normal limits. A repeat series of blood cultures drawn on the 25th hospital day and incubated with penicillinase were sterile. An electrocardiogram and x-ray films of the chest showed no change from those taken at the time of admission. Serum protein electrophoresis determination was approaching normal a week before the patient was discharged, with albumin 4.6 gm and globulin 3.7 gm per 100 ml with a minimal elevation of gamma globulin. The patient remained well during six months of observation after leaving the hospital.

Bacteriological data is presented in Table 1. The colonies were small—0.15 to 0.4 mm in diameter—smooth, glistening and translucent, and they produced an olive green discoloration on the blood agar plate. The presence of 5 per cent carbon dioxide was necessary for maximum growth and in its absence both aerobic and anaerobic cultures grew very poorly. Microscopically, the organisms were Gram-negative, nonmotile short rods and coccobacilli. Optimum growth occurred at 37°C with no growth at 25°C and 42°C.

This organism conforms to Khairat's original description<sup>13</sup> and with the extensive characterization of *H. aphrophilus* by King and Tatum.<sup>14</sup> With minor variations, the organism was similar to that

TABLE 1.—Culture Characteristics and Fermentation Profile of *Hemophilus Aphrophilus* Species Isolated

Blood agar with 5 per cent CO <sub>2</sub> .....	Maximum growth
MacConkey media .....	No growth
SS Media .....	No growth
Leoffler's Media .....	
Pigment .....	Negative
Proteolysis .....	Negative
Catalase .....	Negative
Oxidase .....	Weakly positive
Gelatin .....	Negative
Litmus milk .....	Negative
Citrate .....	Negative
Indol .....	Negative
Urea .....	Negative
Nitrate .....	Negative
Fermentation Base.....	Beef Extract and Serum
Xylose .....	Negative
Mannitol .....	Negative
Salicin .....	Negative
Glucose.....	Acid and gas bubbles 2nd day
Of media + glucose—	
open .....	Acid
closed .....	Acid
Lactose .....	Acid and gas bubbles 2nd day
Maltose .....	Acid and gas bubbles 2nd day
Sucrose .....	Acid and gas bubbles 2nd day

TABLE 2.—Antibiotic Sensitivity Values of *Hemophilus Aphrophilus* Species Isolated

1. Disc Sensitivity (10 microgram discs):		
Penicillin G .....		sensitive
Ampicillin .....		sensitive
Streptomycin .....		sensitive
2. Tube dilution		
sensitivity:	Bacteriostatic level:	Bactericidal level:
Penicillin G.....	0.20 micrograms....	0.80 micrograms
	per cc.	per cc.
Ampicillin .....	Less than 0.10.....	0.20 micrograms
	micrograms per cc.	per cc.
Patient's		
Serum* .....	1:256 dilution .....	1:256 dilution

\*Serum drawn four hours after an ampicillin dose and incubated with organisms isolated from cultures drawn on the fourth hospital day.

described by Russell,<sup>21</sup> who discussed the differential isolation and identification of the Gram-negative pleomorphic bacilli. Table 2 lists antibiotic sensitivity values as well as the patient's serum antibacterial titer. Serum drawn four hours after an ampicillin dose was bactericidal at a dilution of 1:256 against the organism isolated from cultures drawn on the fourth hospital day.

Comment

The U.S. Public Health Service Communicable Disease Center in Atlanta, Georgia, has identified 94 strains\* of *H. aphrophilus* from human infections.<sup>15</sup> Positive cultures have been obtained from the following sources: blood, 43; spinal fluid, 5; brain abscess, 18; sinusitis, 6; finger abscess, 1; superficial skin infections, 11; cervix, 1; chest sinus, 1; thoracentesis fluid, 2; bronchus, 1; peri-appendiceal abscess, 1; unknown, 1. Although the precise number of positive cultures from patients with endocarditis is unknown because case histories are no longer being requested with cultures, the majority of the 43 positive blood cultures were from patients with endocarditis.

It is of interest that in two cases of brain abscess caused by *H. aphrophilus* reported by Fager<sup>3</sup> and by Isom and coworkers,<sup>9</sup> positive cultures were obtained from pet dogs who often licked the patients' necks. The patient in the case herein reported did not have a dog, but often had contact with a poodle belonging to a friend. The poodle often licked the patient on the face and extremities. The dog's saliva was cultured and found negative for *H. aphrophilus*. In addition, the patient's wife and child had throat cultures negative for *H. aphrophilus*.

In six of the nine reported cases of *H. aphro-*

\*As of October 1965.

TABLE 3.—Summary of Clinical Findings in Nine Reported Cases of *H. Aphrophilus* Endocarditis

Patient Reported by Sex	Age	Heart Disease Background	Predisposing Factors	Treatment	Result
Keith and Lyon <sup>12</sup> ..M	66	Rheumatic	Dental extraction	Penicillin, 20 million units for 32 days; streptomycin, 1 gm for 14 days; tetracycline, 2 gm for 3 days; and colistin, 1 gm for 17 days	Cured
Khairat, <sup>13</sup> 1940 ....F	28	Rheumatic	Not stated	Sulfonamides	Died
Quinn, et al. <sup>19</sup> .....M	50	Unknown	None known	Penicillin G, 20 million units for ? days	Died*
Russell, <sup>21</sup> 1965.....M	59	Unknown	Superficial skin infection, left foot	Keflin, <sup>®</sup> 3 gm for 2 days and 2 gm for 14 days, then 1.5 gm for 2 days, relapse, then treated with Keflin, streptomycin and Kanamycin, unknown amounts for 18 additional days	Cured
Toshach and Bain, <sup>23</sup> 1958 .....M	47	?Rheumatic (calcific aortic stenosis)	Heart block, aortic sinus aneurysm	Penicillin, chloramphenicol, chlortetracycline and oxytetracycline	Died
Witorsch and Gordon <sup>26</sup> —					
Case 1, 1955.....F	28	Rheumatic	Upper respiratory	Penicillin, 6 million units for 14 days; probenecid, 2 gm for 14 days, and streptomycin, 1 gm for 14 days	Cured
Case 2, 1963.....M	35	Rheumatic	Dental cleaning	Penicillin, 50 million units for 21 days; streptomycin, 2 gm for 14 days and 1 gm for 7 days	Cured
Case 3, 1963.....M	25	Uncertain	Dermatitis; steroids	Penicillin, 30 million units for 28 days; streptomycin, 1 gm for 30 days; and chloramphenicol, 3 gm for 17 days	Cured
Present case .....M	24	Rheumatic	None known	Penicillin G, 15 million units for 4 days, ampicillin, 12 gm for 29 days, streptomycin, 1 gm for 4 days and 2 gm for 24 days	Cured

\* Bacteriologically sterile at autopsy

*philus* endocarditis cure was obtained with a variety of antibiotics (see Table 3). Khairat's original case occurred before the antibiotic era. Five of the nine patients had had rheumatic heart disease. It seems that the type of bacterial endocarditis caused by this organism is similar to the more common *Streptococcus viridans* variety and tends to attack previously damaged heart valves.

On the basis of in vitro studies of the organism cultured in the present case, one would expect ampicillin to be superior to penicillin G for the treatment of *H. aphrophilus* endocarditis. The report by Quinn and coworkers<sup>19</sup> of a case of *H. aphrophilus* endocarditis treated with ampicillin describes in vitro sensitivities to ampicillin and penicillin G similar to those found in the present case. In their case, the minimum bactericidal concentration for penicillin G was 6.25 micrograms per milliliter compared with 0.049 micrograms per milliliter for ampicillin.

The value of a bactericidal antibiotic in treating bacterial endocarditis has been frequently stressed,<sup>4,6,8,25</sup> and experience in treating infection with other *Hemophilus* species<sup>10,22</sup> would indicate an even greater necessity for a bactericidal drug because of the high relapse rate associated with

*Hemophilus* infections. It was for these reasons that ampicillin in a large dosage was given in the present case. In retrospect, a smaller dose might have been successful, and streptomycin may have been unnecessary.

In a study of review articles\* on bacterial endocarditis published during the last 15 years, covering a total of 1,403 cases, it was noted that there were 10 cases caused by *Hemophilus* organisms excluding the *H. aphrophilus* strain. In addition, Jones<sup>11</sup> found 23 cases of *Hemophilus* endocarditis in his extensive survey of 212 cases of non-streptococcal bacterial endocarditis reported in the world literature between 1936 and 1948. His report included Khairat's case caused by *H. aphrophilus*. These reports,† with a total of 32 cases of *Hemophilus* endocarditis excluding the *aphrophilus* type, suggest that *Hemophilus* organisms rarely cause endocarditis; the total number makes up less than 1 per cent of all bacterial endocarditis. However, when organisms of the *Hemophilus* group are isolated, the *aphrophilus* species should be suspected in view of its increasing frequency of isolation.

\*Reference Nos. 1, 2, 5, 6, 7, 17, 18, 24, 25.

†Reference Nos. 1, 2, 5, 6, 7, 11, 17, 18, 24, 25.



## Summary

In a patient who probably had had rheumatic heart disease, bacterial endocarditis caused by *H. aphrophilus* developed years later. The infection was successfully treated with parenteral ampicillin and streptomycin. Bacteriological data, and in vitro antibiotic sensitivity studies are presented. The eight previously reported cases of bacterial endocarditis caused by this organism are reviewed with treatments compared, including one case treated with ampicillin. The role of this organism in other human infections with the proportion of positive cultures from various sources as confirmed by the Communicable Disease Center, Atlanta, Georgia, is presented. Available data suggest ampicillin is effective in treating infections caused by this organism.

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### GENERIC AND TRADE NAMES FOR DRUGS

Ampicillin—*Polycillin-N*.  
Cephalothin—*Keflin*.

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## Hodgkin's Disease Terminating in Chronic Myeloid Leukemia

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HODGKIN'S DISEASE is an ever popular subject in the medical literature because of its protean manifestations and the diversity of its course. It was first described in 1832 by Thomas Hodgkin as "a disorder affecting the absorbent glands and spleen," and its cause has yet to be determined.<sup>18</sup> Although it is classed with the malignant lymphomas the histologic character of Hodgkin's disease bears

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strong resemblance to an infectious granuloma rather than to a neoplasm.<sup>2</sup> Unlike the other lymphomas it rarely terminates in leukemia. A review of the literature indicates an occasional case report of Hodgkin's disease occurring simultaneously with Kaposi's sarcoma,<sup>4,9</sup> multiple myeloma<sup>8</sup> and with other malignant disorders.<sup>14</sup> Only two cases of myeloid leukemia have been reported

coexistent with Hodgkin's disease.<sup>15</sup> The following case report is of interest because of the relatively long survival of a patient with Hodgkin's disease who later had chronic myeloid leukemia. Whether radiation was a factor in the development of the leukemia will be discussed.

### Report of a Case

A 39-year-old Caucasian housewife noted a left axillary mass in September 1953. Because of fatigability, a 10-pound loss in weight and development of a mass 0.5 cm in diameter in the left clavicular area, she was referred to the University of California Medical Center in February 1954. The mass was removed and microscopic examination showed replacement of the usual lymph node architecture by reticulum cells and a profusion of Reed-Sternberg cells typical of Hodgkin's granuloma (Figure 1). An x-ray film of the chest showed a small left pleural effusion and a large lobulated anterior mediastinal mass (Figure 2). An abdominal scout film showed obliteration of the right psoas shadow, hepatomegaly and an enlarged spleen. Leukocytes numbered 12,750 per cu mm and hemoglobin concentration was 70 per cent. Radiation therapy was begun 2 March 1954. A detailed account of the courses of radiation is given in Table 1. A tumor dose of 1,000 r was given to the mediastinum and a tissue dose of 1,500 r to the left axilla. Follow-up appointments in the outpatient clinics showed progressive decrease in adenopathy (Figure 3) and on 9 December 1964, physical examination was within normal limits. In June 1955, a 4 × 4 cm left supraclavicular node was noted; 1,000 r was given and the node promptly disappeared. In August 1956, right cervical adenopathy appeared and it also responded to radiation therapy. The patient

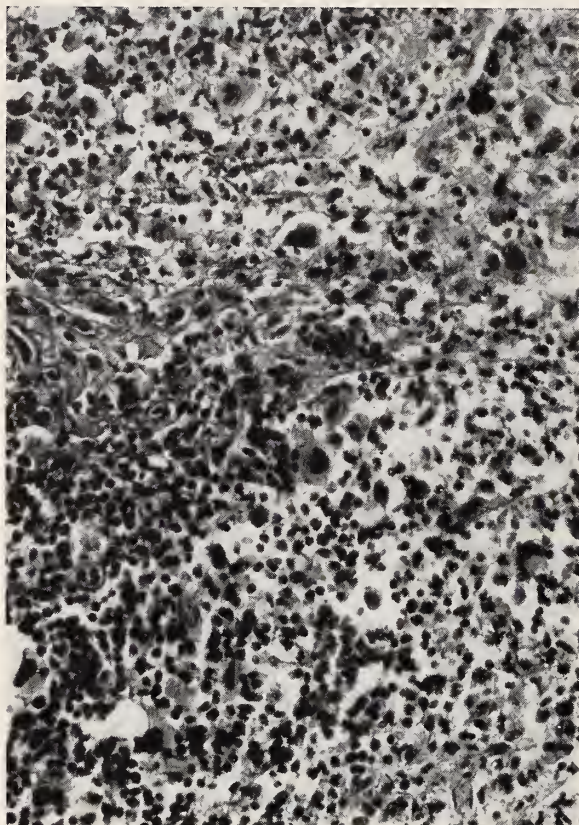


Figure 1.—Section showing replacement of usual lymph node architecture by reticulum cells with a mixture of lymphocytes, eosinophils, polymorphonuclear cells, plasma cells and a profusion of Reed-Sternberg cells (Hematoxylin eosin stain, ×250).

TABLE 1.—Details of X-Radiation

Date	Number of Treatments	Location	Field	r in Air	r to Skin	r to Tissue Calculated at 3 cm in Depth
3/2/54-3/23/54.....	16 (22 days)	Anterior mediastinum	10×15 cm	1,700	2,500	1,000 (tumor)
		Posterior mediastinum	10×15 cm	700	900	
3/16/54-3/25/54.....	8 (10 days)	Left axilla	10×10 cm	1,500	1,900	1,500 (tissue)
6/13/55-6/18/55.....	6	Left supraclavicular	7×7 cm	1,100	1,350	1,000 (tissue)
8/2/56-8/ 7/56.....	5	Right cervical	7×7 cm	1,100	1,350	1,000 (tissue)
10/7/60-12/3/60.....	31 (44 days)	Right supraclavicular	9×13 cm	5,048	5,550	4,455 (midplane)
	32 (47 days)	Right axilla	9×9 cm	4,982	5,450	
	40 (59 days)	Anterior mediastinum	20×9 cm	5,088	5,700	
		Posterior mediastinum	20×9 cm	3,392	3,800	

Technical factors: 250 KVP, 30 MA, 1.4 mm. CU HVL, 50 cm. TSD, 0.5 mm. CU + 1.0 mm. AL filter. Tumor dose equals dose at the midplane. Tissue dose calculated at 3 cm in depth.





Figure 2.—Roentgenogram of the chest, 17 February 1954, showing a large lobulated anterior-superior and anterior-middle mediastinal mass.



Figure 3.—Roentgenogram of the chest two months after completion of initial course of radiation therapy, showing complete regression of the mediastinal mass.

was seen every two months and remained asymptomatic with no abnormality noted on physical examination, blood studies or roentgenograms of the chest until 30 June 1960, when an x-ray film showed mediastinal widening, and a right axillary node was palpable. Radiation therapy was given to the right axilla and to the mediastinum during the fall of 1960.

The patient felt well, and physical examination and hemogram were normal until June 1961, when leukocytes numbered 18,500 per cu mm. She was seen at monthly intervals thereafter until October 1961, when she was admitted to the Cancer Research Institute of the University of California Hospitals because of progressive in-

crease in the leukocyte count. Hematologic changes are listed in Table 2.

On admission to the hospital she appeared well developed and well nourished and was without symptoms. There was radiation erythema over the chest, back, arms and neck. A  $0.5 \times 1$  cm left supraclavicular node was palpable. There was no sternal tenderness. The spleen was palpable 3 cm below the left costal margin. The remainder of the physical examination was normal. Laboratory studies showed leukocytes numbering 132,600 per cu mm, the hematocrit at 35 per cent, and platelets numbering 835,000 per cu mm with many large bizarre forms. Urinalysis was within normal limits. Results of a bromsulphalein test and of determinations of blood chemical factors, including calcium, phosphorus, glucose, creatinine and serum protein, were within normal limits. The uric acid content was 8.1 mg per 100 ml. The leukocyte alkaline phosphatase was 2 per cent positive. Papanicolaou studies of cervical smears were negative for neoplasm. An intravenous pyelogram showed a normal urinary collecting system; enlargement of the liver and spleen was noted. An x-ray film of the chest showed slight prominence of the right superior mediastinum. A bone survey was negative for metastatic disease. Marrow aspirated from the iliac crest showed increase in the myeloid series with an increase in promyelocytes. A diagnosis of chronic granulocytic leukemia was established and on 8 November 1961 treatment with busulfan (Myleran®), 2 mg twice a day, was begun.

The patient was observed at regular intervals in the Cancer Research Outpatient Clinic and she responded well to busulfan therapy. Except for herpes zoster developing at the level of the twelfth thoracic vertebra in December 1962, the patient felt well and had no other complications until October 1963, when it was noted that the hematocrit was gradually decreasing. On 13 November 1963 she was admitted to the Cancer Research Institute because of fatigue, frequent colds and edema at the ankles. She was alert and pale but apparently in no distress. There was no enlargement of nodes. The liver was palpable 7 cm below the right costal margin and the spleen 3 cm below the left costal margin. There was 3 plus pedal edema.

The hematocrit was 20.5 per cent. Leukocytes numbered 12,150 (54 per cent polymorphonuclear, 16 per cent band cells, 5 per cent meta-

TABLE 2.—Hematologic Data for Last Three Years of Patient's Life

Date	Leukocytes (per cu mm)	Hgb (gm per 100 ml)	Hematocrit (Vol per cent)	Lymph Per Cent	PMN's Per Cent	Nonseg Per Cent	Eos Per Cent	Baso Per Cent	Mono Per Cent	Meta Per Cent	Myelo Per Cent	Promyel Per Cent	Platelet per cu mm <sup>3</sup>
10/10/60.....	7,900	12.8	42	12	76	....	1	....	11	....	....	....	adequate
11/13/60.....	5,400	12.8	40	3	81	1	3	....	12	....	....	....	adequate
12/15/60.....	6,500	11.6	35	....	....	....	....	....	....	....	....	....	.....
3/16/61.....	7,500	11.6	.....	....	....	....	....	....	....	....	....	....	.....
6/15/61.....	18,500	11.9	.....	....	....	....	....	....	....	....	....	....	.....
6/28/61.....	22,850	11.4	.....	32	63	1	1	2	1	....	....	....	.....
7/27/61.....	31,500	12.9	41	16	63	7	5	4	5	....	....	....	adequate
8/10/61.....	45,500	12.3	41	5	66	10	1	3	3	8	4	....	.....
9/26/61.....	92,000	11.4	41	....	....	....	....	....	....	....	....	....	.....
10/31/61.....	132,600	11.5	35	1	38	25	2	3	3	22	5	1	835,000
11/ 8/61.....	148,500	11.3	34	1	33	14	1	5	1	36	7	2	1,245,000
11/16/61.....	152,000	10.2	34	....	34	23	4	4	1	16	11	7	1,075,000
11/30/61.....	64,175	10.9	.....	2	52	11	2	4	....	6	5	18	745,000
12/14/61.....	25,500	10.8	36.7	1	72	6	4	8	5	....	....	4	815,100
12/28/61.....	13,700	11.2	36.1	1	75	6	3	2	4	6	2	1	467,000
4/19/62.....	8,450	13.5	43.5	6	83	3	3	4	1	....	....	....	415,000
7/12/62.....	31,650	13.8	46	....	71	3	4	1	1	10	10	....	665,000
9/ 6/62.....	34,250	14	41.5	2	56	17	2	3	1	10	2	7	2,295,000
10/18/62.....	16,050	12.5	37.6	5	76	3	2	4	3	3	4	....	869,000
12/27/62.....	18,450	13.3	41.2	4	71	5	4	5	8	1	2	....	1,000,000
2/ 7/63.....	7,900	11.5	37.2	....	....	....	....	....	....	....	....	....	.....
2/21/63.....	6,850	11.6	35.2	....	....	....	....	....	....	....	....	....	.....
3/ 7/63.....	10,000	11.8	37.8	....	....	....	....	....	....	....	....	....	.....
6/ 4/63.....	20,550	11.9	37.8	2	82	4	1	2	2	5	1	1	1,376,000
8/27/63.....	11,600	12.2	40	3	73	3	1	6	6	2	4	2	424,000
9/10/63.....	9,600	11.8	37.5	3	57	3	5	11	14	5	1	1	455,000
10/ 8/63.....	28,100	10.6	35.2	1	41	6	3	10	4	9	13	13	620,000
10/22/63.....	27,550	8.7	28	6	43	1	7	3	4	6	20	10	315,000
11/12/63.....	15,200	6.9	20	8	36	8	3	4	....	6	25	10	300,000
12/ 5/63.....	30,350	7.8	24.5	1	24	5	3	4	1	25	30	7	650,000
12/12/63.....	14,850	6.0	18.4	2	30	10	6	....	2	11	22	7	334,000
12/26/63.....	3,100	....	....	4	64	3	2	1	....	15	10	1	.....



myelocytes, 7 per cent myelocytes, 10 per cent promyelocytes, 3 per cent eosinophils, 1 per cent basophils, 3 per cent lymphocytes, 1 per cent monocytes) and platelets 499,000 per cu mm. The urine showed a trace of protein and there were 15 to 20 leukocytes per high power field. The serum protein was 5.4 gm per 100 ml with an electrophoretic pattern showing a decrease in the albumin component (53.2 per cent). The bilirubin was 0.2 mg, calcium 8.8 mg, phosphorus 4 mg, uric acid 5.6 mg, and blood urea nitrogen 11.4 mg per 100 ml. Bromsulphalein retention was 10 per cent in 45 minutes. The serum iron was 81 mcg per 100 ml, with total iron-binding capacity of 254 mcg per 100 mg. The result of a Coombs' test (direct and indirect) was negative. The urobilinogen content of the stool was 111 mg in 72 hours. An erythrocyte survival determination with Cr<sup>51</sup> showed a half-time of 17.5 days (normal 25 to 40 days). Erythrocyte cholinesterase was 1.17 units (normal 0.80 to 1.20). Marrow aspirated from the iliac crest showed generalized hypoplasia with a decrease in the erythrocytic precursors and megakaryocytes. The predominant cell type was a myelocyte. There was no significant shift to the left. A roentgenogram of the chest showed a slightly widened right paratracheal shadow and an increase in the size of the heart.

It was the consensus that the patient had chronic granulocytic leukemia with diminished red blood cell production and that a hemolytic component also was playing an etiologic role in the anemia. A transfusion of two units of whole blood was given and treatment with 6-mercaptopurine, in dosage of 50 mg a day, was begun just before the patient was discharged from the hospital 30 November 1963. When she returned to the clinic on 12 December 1963, the hematocrit was 18.4 per cent. Prednisone, 60 mg per day, was started. Two weeks later the hematocrit was still low and the leukocyte count had dropped to 3,100 per cu mm with no significant increase in immature forms. Prednisone was continued but the use of 6-mercaptopurine was stopped.

The patient died at home on 1 January 1964. Permission for autopsy was not granted.

## Discussion

It has been recognized that the malignant lymphomas (lymphosarcoma, reticulum cell sarcoma, giant follicular lymphoblastoma and Hodgkin's disease) and lymphatic leukemia are closely re-

lated. Sternberg, in 1908, recognized "leukemic blood" in cases of lymphosarcoma, and transition forms from one to another have been encountered.<sup>1</sup> The incidence of leukemic transition in a series of 1,269 patients with lymphosarcoma has been reported as 7.6 per cent.<sup>16</sup> There are few reports of leukemia, other than lymphatic leukemia, occurring spontaneously in lymphoma; the reported cases have usually followed radiation therapy.<sup>3,11,19</sup>

That radiation exposure in man is associated with an increased incidence of leukemia has been well documented.<sup>6,10,13</sup> Analysis of persons exposed to atomic radiation<sup>12</sup> and patients irradiated for ankylosing spondylitis<sup>7</sup> indicates that acute leukemia and chronic myeloid leukemia may be caused by radiation under certain conditions. There is some evidence that fractionated and repeated irradiation may be more leukemogenic than that given in a single episode.<sup>17,20</sup> When leukemia is related to radiation, at least 12 to 18 months elapse between irradiation and onset of leukemia.<sup>5</sup>

In the case here reported, radiation therapy was begun in March 1954 and intermittent courses were given until December 1960. The peripheral blood remained normal until June 1961. It is believed that the terminal illness was due to cumulative effects of radiation therapy rather than to a spontaneous occurrence. The development of myeloid leukemia in patients with Hodgkin's disease who have not received irradiation is so rare that it can be considered fortuitous. Both the literature and the present case suggest that myeloid leukemia in patients with Hodgkin's disease is related to therapeutic exposure to x-rays.

Although radiation is curative in localized Hodgkin's disease and is certainly the treatment of choice initially, discretion should be used in the total amount administered.

## Summary

A case in which a patient with Hodgkin's disease was treated with high dose radiation therapy is reported. After seven and a half years of satisfactory control, chronic myeloid leukemia developed. The patient at first responded well to Myleran<sup>®</sup> therapy but after 23 months refractory hemolytic anemia developed and the patient died.

It is postulated that the development of chronic myeloid leukemia was a consequence of the radiation therapy.

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Busulfan—*Myeleran*.

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## Tuberculous Tenosynovitis In a Patient with Hyperuricemia

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TUBERCULOUS TENOSYNOVITIS is uncommon. Even when tuberculosis was highly prevalent, Adams and coworkers<sup>1</sup> found that during a 45-year period only 36 patients were admitted to the Massachusetts General Hospital with this disease (one case per 7,891 admissions). Although the incidence of tuberculosis has decreased dramatically since the advent of anti-tuberculosis drugs, tuberculous tenosynovitis still occasionally occurs and may mimic the more frequently seen metabolic or rheumatic diseases.

### Report of a Case

A 53-year-old white woman was first seen at the University of California Surgical Clinic in April 1964 because of recurrent swellings and masses on the left hand and wrist. The swelling had been present since December 1961, and was associated with throbbing pain, loss of sensation in the fingertips and weakening of grasp. The patient had been treated with cortisone by another physician but with only slight improvement.

In July 1962 painless masses appeared on the dorsal and volar aspects of the wrist, hand and dorsal forearm. Biopsy showed widespread granulomata, Langhans' giant cells and epithelioid cells compatible with tuberculosis or sarcoid. She had no history of pulmonary tuberculosis but she had drunk raw milk when she was a child and had a 30-year history of pain, crepitus and limitation of motion of the left hip. She had had stage II carcinoma of the cervix 10 years previously, which was treated by radium. She was treated with strep-

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Figure 1.—Tenosynovitis of the volar and dorsal aspects of hand and wrists. Roentgenogram shows soft tissues and no bony destruction.

tomyacin from December 1962 to August 1963, when the drug was discontinued because of an adverse reaction. The swellings and masses diminished; she became asymptomatic, and did not return to her physician.

Two months later she saw another physician because of recurrence of painful swelling and masses on the dorsum of the left forearm, wrist and hand, together with severe back pain. Laboratory studies on 8 November 1964 showed: uric acid 14.0 mg per 100 ml and cholesterol 221 mg per 100 ml, alkaline phosphatase 4.7 Bodansky units and hemoglobin 13.2 gm per 100 ml. Leuko-

cytes numbered 9,000 per cu mm with 78 segmental neutrophils and 22 per cent lymphocytes. Urinalysis was normal.

Radiologic studies showed a loss of disk space, destruction of vertebral bodies of the ninth and tenth thoracic vertebrae, and destructive changes in the left acetabulum and femoral head.

Metastatic disease was suspected because of the previous history of cervical carcinoma. However, there was no evidence of recurrence, and the patient's physician attributed the symptoms and findings to an atypical gouty arthritis. She was treated with a phenylbutazone-cortisone preparation and the serum uric acid fell to 11.7 mg per 100 ml three weeks later and to 8.6 mg after five weeks. The symptoms lessened and the patient did not return for follow-up examinations although she continued to take the prescribed preparation.

She came to the University of California Surgical Clinic in April 1964 because the masses and swellings of the left upper extremity did not subside with treatment. She walked with an antalgic gait, and her left leg was conspicuously shorter than the right. She had a non-tender depression over the ninth thoracic vertebra. Prominent, non-tender, doughy, slightly fluctuant, saccular swellings were present over both dorsal and volar surfaces of the left wrist and hands (Figures 1 and 2). The palmar curve was flattened, and hour-glass-shaped volar masses were present which moved with flexor-tendon motion.

Laboratory studies showed a hematocrit of 45 per cent, a sedimentation rate of 18 mm in one hour (Wintrobe) and leukocyte count of 9,000 per cu mm with a cell differential within a normal range. The serum creatinine was 0.8 mg, serum uric acid 3.1 mg, calcium 9.8 mg, phosphorus 3.3 mg and total protein 7.6 gm per 100 ml. Alkaline phosphatase was 3.0 Bodansky units. Urinalysis showed 30 white blood cells per high power field. No abnormality was seen on examination of a cervical smear. An intermediate purified protein derivative tuberculin skin test was borderline positive. No abnormality was observed on an intravenous pyelogram. Needle aspiration of synovial swellings on the dorsum of the hand produced a thick, tenacious, clear yellowish fluid which was negative for uric acid crystals when examined microscopically with polarized light. A direct smear was negative for organisms but a culture was positive for mycobacterium tuberculosis.



Figure 2.—Roentgenograms showing tuberculous destruction of left hip and ninth and tenth thoracic vertebrae.

Radiologic studies of the hands showed soft tissue swelling, but no destructive joint or bony changes. No significant changes were seen in the lesions of the vertebrae and hip when compared with roentgenograms taken five months before. These lesions were thought to be compatible with active tuberculosis. Roentgenograms of the chest and tomograms showed only a few old nodular densities and fibrotic streaks.

The patient at first declined treatment and did not return to the clinic until August 1964, when she was given daily doses of isoniazid, 300 mg, and para-aminosalicylic acid 12 gm. She was admitted to the University of California Hospital in October 1964. A thick yellow purulent material was aspirated from the ninth and tenth thoracic vertebrae, and a spinal fusion was performed. Three weeks later the swollen synovial sheaths on the dorsum of her left hand were dissected and excised from the extensor tendons. The pathologic report was granulomatous tenosynovitis. Acid-fast stains were negative. After an uneventful postoperative course, the patient was discharged, to be followed in the clinic and to continue the anti-

tuberculosis chemotherapy that was started before operation.

## Discussion

In the case here reported, hyperuricemia and recurrent painful swellings and lumps on the hands and wrists led to an initial diagnosis of gout. The clinical improvement and the decreased serum uric acid after treatment with phenylbutazone and prednisone supported this diagnosis. However, the absence of uric acid crystals and the demonstration of mycobacterium tuberculosis in the synovial lesions confirmed the tuberculous nature of the lesions. So far as could be determined, the coexistence of hyperuricemia and tuberculous tenosynovitis has not been previously reported.<sup>12,13,14,15</sup> The patient in the present case had none of the diseases that are more commonly associated with hyperuricemia, such as renal insufficiency, blood dyscrasias (polycythemia vera, leukemia, myeloid metaplasia), lymphoma or other neoplastic diseases, diabetes mellitus, hyperparathyroidism or hypoparathyroidism or myxedema nor was there a history of ingestion of such drugs as pyrazinamide, chlorothiazide and acetazolamide. Although acute bacterial infection may provoke an attack of gout in a known gouty patient,<sup>12</sup> it has not been reported to cause hyperuricemia in an otherwise normal person. There was no clinical evidence of gout in the present case (it has been reported that fewer than 5 per cent of patients with gout are females<sup>14</sup>). The relationship of the hyperuricemia and the tuberculous tenosynovitis is at best speculative in this case.

The most common symptoms of tuberculous tenosynovitis are swelling of synovial-lined spaces in the hand and wrist, occasional crepitation, numbness and weakness. The average duration of symptoms is 45 months.<sup>2</sup> Pulmonary and osseous tuberculosis may occur in the patients, but many of them have only tenosynovitis.<sup>1-11</sup> Diagnostic studies in patients with suspected tuberculous tenosynovitis should include tuberculin and fungal skin tests, radiologic studies of the chest and affected parts, bacteriologic study of aspirated fluid (from swollen synovia) and histologic examination of the synovial sheath.<sup>2,5</sup> Treatment consists of radical excision of involved tendon sheaths, bursae and involved surrounding tissues.<sup>1-11</sup> Preoperative and postoperative anti-tuberculosis chemotherapy (isoniazide, para-aminosalicylic acid and streptomycin) is given in standard doses. Conservative



measures usually are not successful<sup>1-13</sup> although exceptions have been reported.<sup>10</sup>

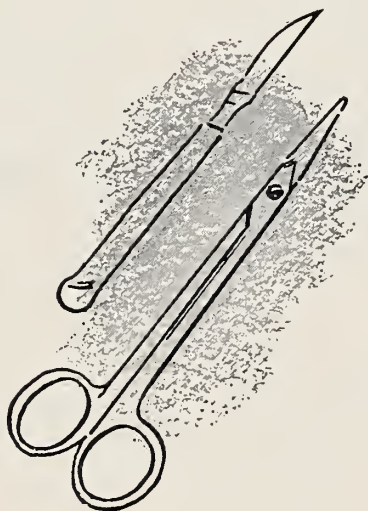
### Summary

A 53-year-old woman had tenosynovitis and hyperuricemia. She had no documented clinical evidence of gout, and mycobacterium tuberculosis was demonstrated in the synovial swellings. Although the incidence of tuberculosis has greatly decreased, it still occurs and may mimic other more common diseases.

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# Acute Intermittent Porphyrria

*These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Assistant Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.*

DR. JOSEPH S. GOLDBERG:\* Today's first case is that of a 50-year-old hotel manager with intermittent attacks of abdominal pain. The patient felt perfectly well until about six years ago when severe, intermittent, mid-epigastric pain, associated with nausea, vomiting, constipation and back pain first occurred. These attacks were occasionally precipitated by heavy ingestion of alcohol and would last between one day and three months. For the past two years, the patient has noticed the passage of dark red urine during the attacks. The family history was non-contributory. The past medical history was significant in that the patient had had only one operation, for hernia repair seven years before admission.

The patient was moderately obese and the vital signs were normal. On examination of the abdomen mid-epigastric tenderness was noted on pressure but not on rebound. The liver was felt 2 to 3 cm below the right costal margin. Results of examination of the skin and of neurological examination were within normal limits.

Laboratory examination: Hemoglobin, leukocyte count and differential and urinalysis were within normal limits. The Watson-Schwartz test for porphobilinogen was strongly positive (Table 1). Twenty-four-hour urinary excretion of coproporphyrins and uroporphyrins was greatly elevated. The two-hour post-prandial blood sugar

was 90 mg per 100 ml. Serum creatinine was 1.5 mg and serum bilirubin 0.8 mg per 100 ml. Serum glutamic-pyruvic transaminase was 58 units (normal 5 to 35 units), and alkaline phosphatase was 3 Shinowara-Jones-Reinhart Units (SJR) (normal 2 to 6 SJR units). The prothrombin time, thymol turbidity and cephalin flocculation test were within normal limits. No abnormality was noted on x-ray films of the chest but on x-ray examination of the abdomen changes compatible with paralytic ileus were observed.

DR. LLOYD H. SMITH, JR.:† The patient under discussion quite clearly has acute, intermittent porphyria. It should be noted that this disorder is misnamed, for it is not really "acute and intermittent," in that it is a genetic disease presumably

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TABLE 1.—The Watson-Schwartz Test

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Method—

- Step 1—Add 2.5 ml Ehrlich's reagent to 2.5 ml of freshly voided urine and shake well
- Step 2—After exactly 15 seconds, add 5 ml of saturated sodium acetate
- Step 3—Add 5 ml of chloroform. Shake well and centrifuge

Interpretation—

A positive result is a definite red color in the aqueous or upper phase. False positive reactions may be caused by indoles, anticonvulsant drugs, and pyridium

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present since conception. Nor is it basically porphyria according to current concepts of the chemical derangement, as will be noted later. In this particular patient, acute intermittent porphyria (AIP) has been manifested clinically only by attacks of the typical abdominal pain. He has so far been spared severe neurological abnormalities, which sometimes are fatal. The diagnosis has been adequately established by demonstration of excessive urinary porphobilinogen (Watson-Schwartz test). In our discussion today we shall be unable to survey the total array of disorders characterized by abnormalities of porphyrin metabolism. Major attention will be directed toward the metabolic defect of AIP.

We all have "porphyria." As in so many other metabolic diseases, an abnormality of porphyrin metabolism is a matter of degree. The porphyrins are very important compounds in biology, representing not only the heme in hemoglobin but also the prosthetic groups of myoglobin, catalase, cytochromes and peroxidase. Other important related compounds are vitamin B<sub>12</sub> and chlorophyll. In man, at least 300 mg of porphyrins are synthesized every day. This represents a minimal figure, the amount necessary for the replacement of the heme in hemoglobin. An unknown additional amount is necessary to provide for porphyrin turnover in other enzymes. In this discussion of porphyrin metabolism, we are considering the afferent arm, if you will, of tetrapyrrole synthesis. In contrast, last week at these Grand Rounds exercises we discussed abnormalities in bilirubin metabolism

[CALIFORNIA MEDICINE, February 1966], representing the breakdown, conjugation and excretion of the porphyrins (Chart 1).

### Biochemistry of the Porphyrin

The porphyrins are composed of four pyrrole rings held together in methylene linkage. A review of porphyrin biochemistry is necessary for understanding current concepts concerning pathogenesis of the porphyrias. The pyrrole ring is synthesized from very simple precursors, glycine and succinate, and then is assembled into the specific tetrapyrrole. The first step unique to porphyrin biosynthesis is the formation of delta aminolevulinic acid (ALA) from the enzymatic condensation of the B<sub>6</sub> derivative of glycine and succinyl coenzyme A (Chart 2). At least two co-factors are necessary: pantothenic acid for the synthesis of coenzyme A and vitamin B<sub>6</sub> as a precursor of pyridoxal phosphate. Biotin may also be involved in this reaction, although so far this evidence has been obtained primarily from studies of microorganisms. The enzyme catalyzing this reaction, delta aminolevulinic acid synthetase, is a particulate enzyme and is lost from the maturing red cell. More important, it is the site of feedback inhibition controlling the rate of porphyrin synthesis, as we shall comment upon later. Delta aminolevulinic acid may contribute its terminal carbon to the one-carbon pool, by the Shemin pathway, and in this way contribute to purine biosynthesis. Evidence suggests that this pathway is not of great quantitative importance in man. How much ALA

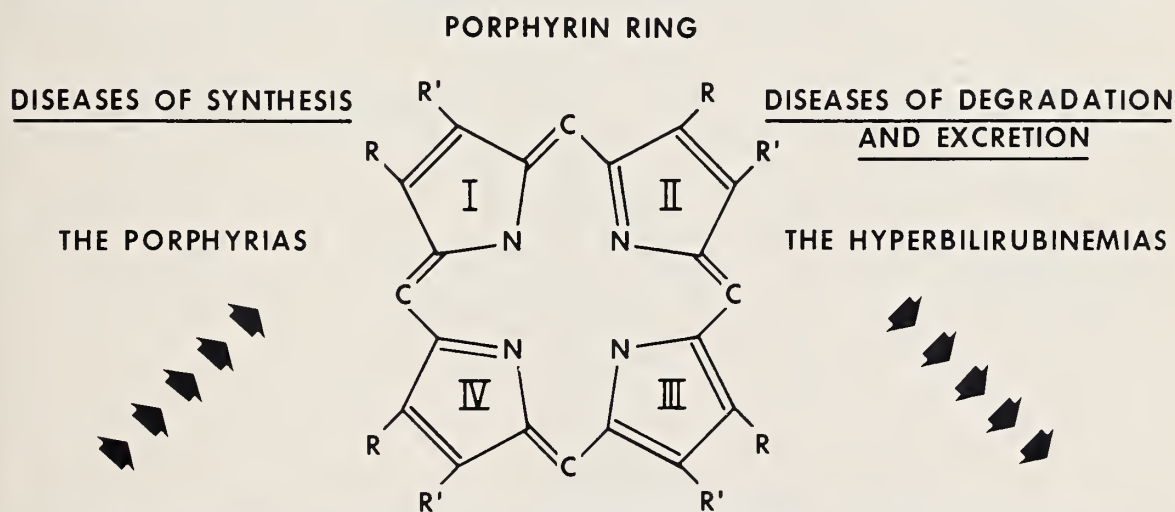


Chart 1.—Diagram of the porphyrin ring and the relationship of the porphyrias to the hyperbilirubinemias.

is normally formed? Probably around 400 to 500 mg a day. Of this, only one or two milligrams is normally lost as a colorless compound in urine. The remaining ALA is presumably converted to porphobilinogen.

Porphobilinogen (PBG) represents the first completed pyrrole ring. It is formed by the condensation of two molecules of ALA (Chart 3). The molecules are overlapped and two molecules of water are removed by a dehydrase reaction to form the pyrrole ring. You will note that the PBG has two side chains, an acetate and a propionate, both derived from succinic acid. I will subsequently speak of these as the "A" and "P" side chains. As in the case of delta aminolevulinic acid, most of the PBG that is formed (perhaps 400 mg) continues down the pathway of porphyrin biosynthesis, and, once again, only a very small fraction, less than 1 per cent (one or two milligrams), is lost in the urine. If PBG is present in pronounced excess, it is the source of the positive reaction to the Watson-Schwartz test, such as occurred in the present case.

The linkage of four porphobilinogen rings to

form a tetrapyrrole is, at best, a somewhat murky area. I shall try not to complicate this unnecessarily for those not enamoured of porphyrin chemistry. The first step is thought to be that of the loss of the amine group from the side chain forming an unknown intermediate—possibly a tetrapyrrole, possibly a dipyrrole (Chart 4). It is apparent that there are four different ways in which four pyrrole rings could condense to form a porphyrin. It is quite fortunate for our sanity that only two of these are found in nature. In the first, you see that the "A" and "P" groups derived from PBG are in regular sequence around the tetrapyrrole. This regular alternation of acetyl and propionic groups is the Type I porphyrin sequence. The first compound formed is uroporphyrinogen Type I. Less than 1 per cent of the porphyrin synthesized goes down the Type I pathway. This has no usefulness as far as we know and presumably represents some form of chemical slippance. Most of the unknown tetrapyrrole intermediate is acted upon by an additional enzyme, uroporphyrinogen isomerase, which results in a side chain sequence, which we may think of as

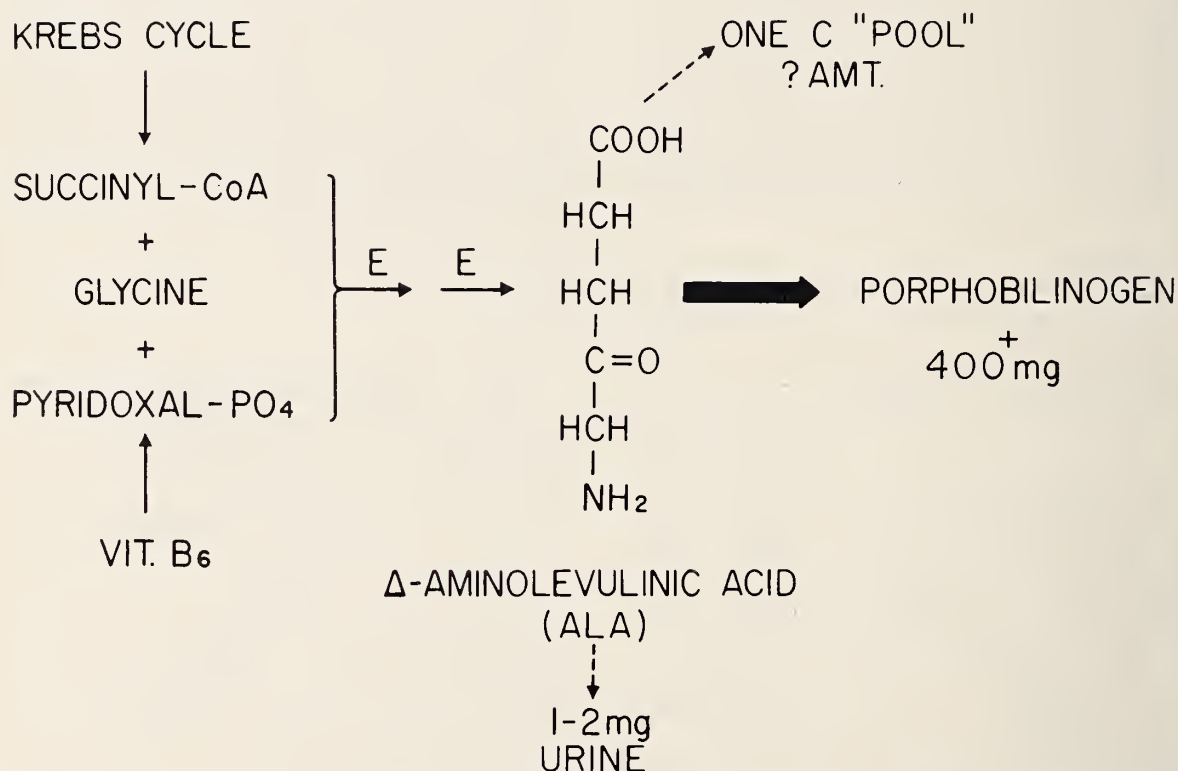


Chart 2.—Formation of delta aminolevulinic acid from the enzymatic condensation of the B<sub>6</sub> derivative of glycine and succinyl coenzyme A. This step is catalyzed by delta-aminolevulinic acid synthetase.



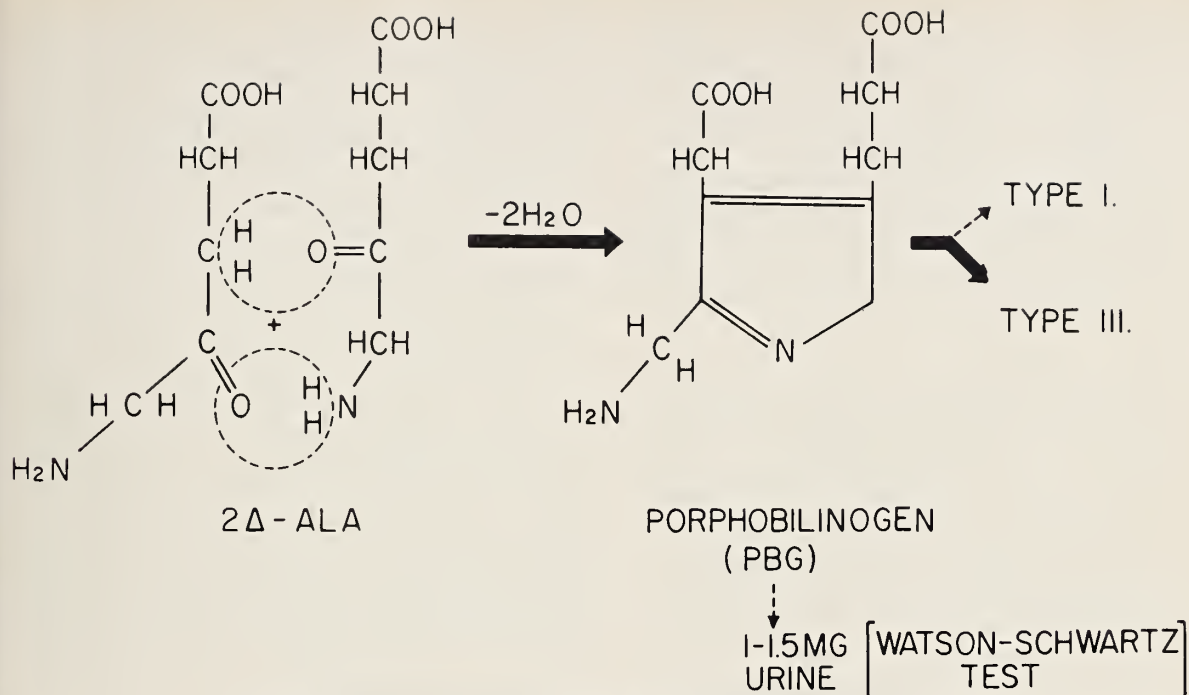


Chart 3.—The first completed pyrrole ring—porphobilinogen (PBG).

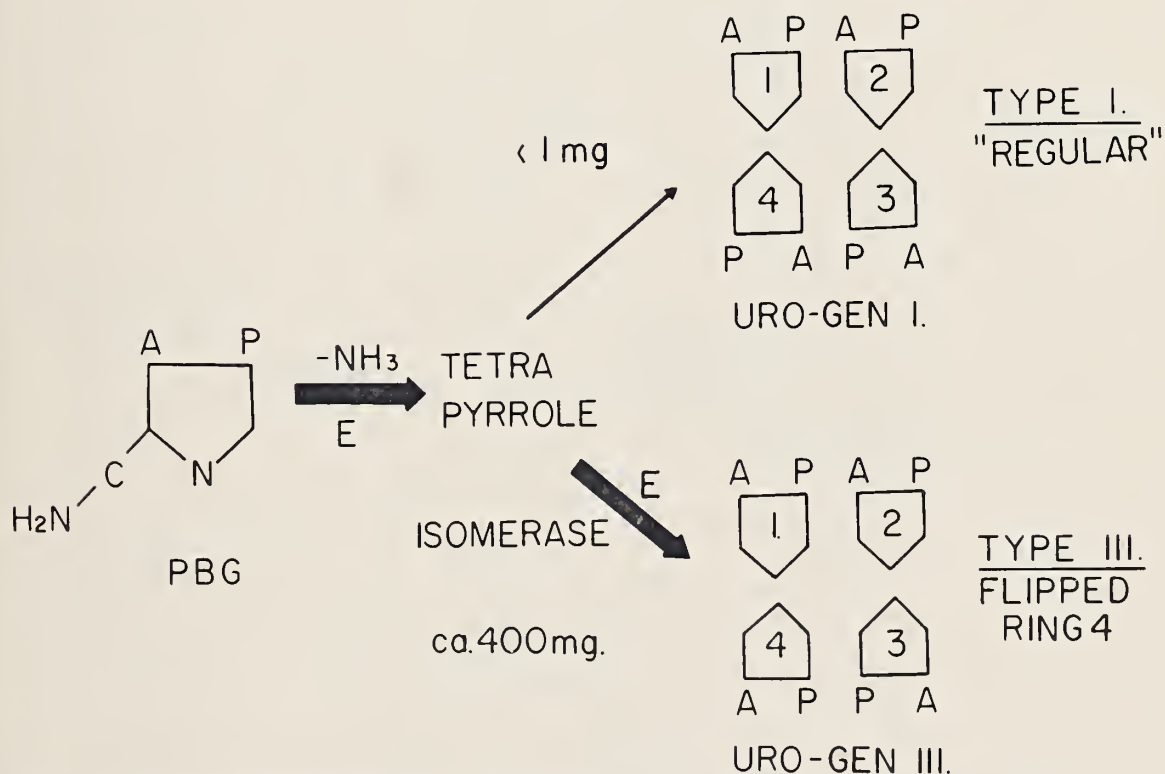


Chart 4.—The first step in the linkage of four porphobilinogen rings forms a tetrapyrrole (possibly a dipyrrole), which is converted to uroporphyrinogen Type I or Type III.

the "flipped fourth ring." The sequence is regularly "A"- "P" through ring three, but when one gets to the fourth ring it is as if the pyrrole ring were picked out, turned over, and put in a backward sequence, so that one has "P"- "A."

In summary, only two types of porphyrins are found in nature: Type I, with a regular side chain sequence, and Type III, with a flipped fourth ring. The Type III pathway is the one necessary for the normal synthesis of biologically active porphyrin.

The second point to be brought out is that the porphyrins themselves are not synthesized as the primary products, but rather the porphyrinogens, which are colorless compounds with reduced methylene bridges. These are readily oxidized to the colored porphyrins which are found in urine. Most of the uroporphyrinogen is converted to the coproporphyrinogen by the sequential decarboxylation of the acetyl groups yielding methyl groups (Chart 5). In the Type I series, this is the end of the road. There is no step beyond the coproporphyrinogen I, and the reduced precursors are

oxidized to form the colored porphyrins, uroporphyrin I and coproporphyrin I, which are excreted unaltered in urine and feces. In the Type III pathway, however, the coproporphyrinogen Type III can be further altered enzymatically with conversion of two of the propionic acid residues to vinyl groups (designated as V in Chart 5), forming protoporphyrinogen. Its oxidized form, protoporphyrin, accepts iron to form heme.

I think that we can illustrate this somewhat complicated pathway by drawing a very simplified diagram (Chart 6), showing the precursors glycine and succinate and the main pathway of porphyrin synthesis terminating in heme. Along this pathway certain porphyrins and porphyrin precursors are lost from the cells and excreted in urine or feces. How much is lost normally? Approximately one to two milligrams of delta aminolevulinic acid and a similar quantity of porphobilinogen are excreted in the urine. None is found in the feces. Uroporphyrin is found in the urine (0 to 30 micrograms a day) but not in the feces. Coproporphyrin normally appears both in the

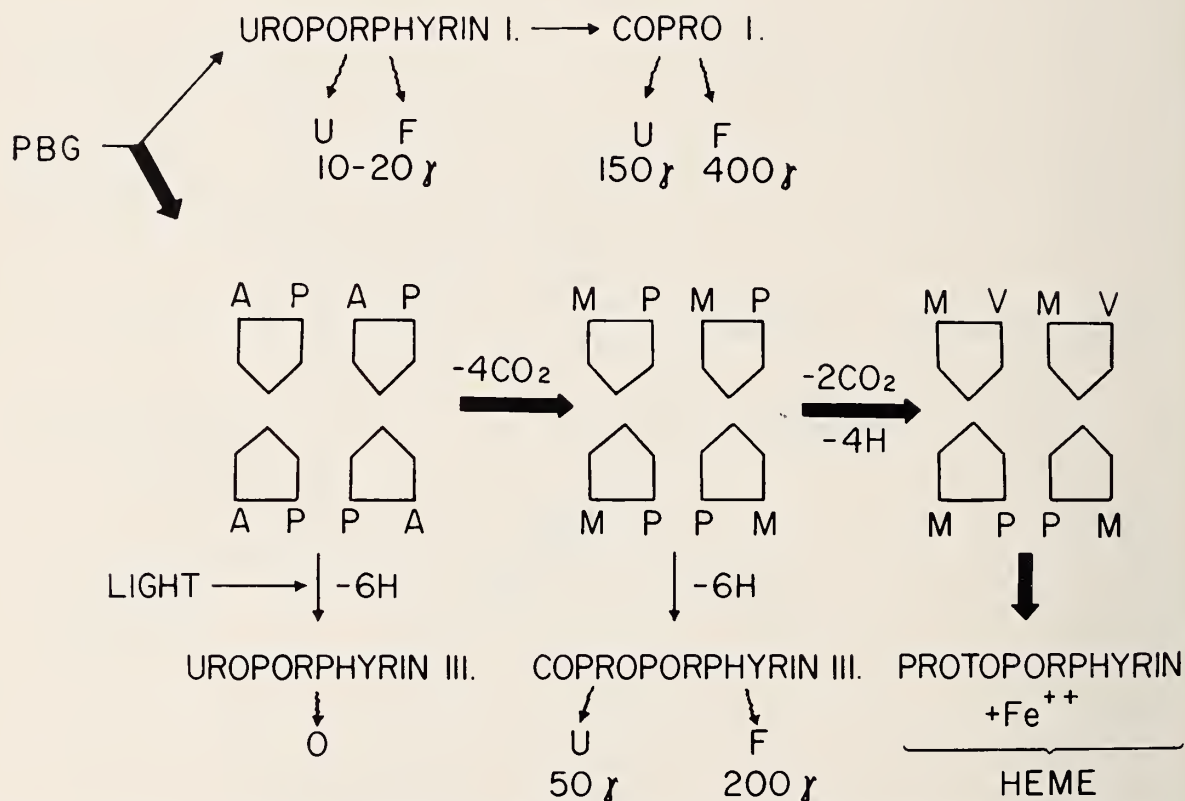


Chart 5.—The conversion of uroporphyrinogen to coproporphyrinogen occurs by the sequential decarboxylation of the acetyl groups yielding methyl groups; M, methyl; P, propionic; V, vinyl.



urine (100 to 300 micrograms) and in the feces (400 to 1,000 micrograms). Protoporphyrin is not found in urine but is excreted in feces. The figures vary considerably but are in the range of 500 to 1,200 micrograms a day. It will be noted that the porphyrin precursors and uroporphyrins are more water-soluble and tend to appear in urine. As protoporphyrin is approached, they become more lipid-soluble and appear in bile and feces. The pathway is very efficient in that only 1 per cent of the numerous intermediates is lost.

### Diseases of Porphyrin Metabolism

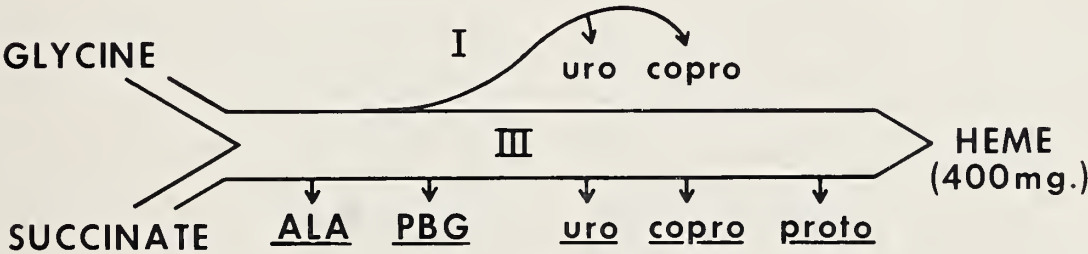
What diseases of porphyrin metabolism occur? Those who are brave enough to attempt classifications of porphyria agree only on one thing—that the schemes put forward by their colleagues are inadequate to encompass all the cases seen. That will be true of the simplified classification given here, which might be called “Remington eclectic”

(Table 2). In the erythropoietic porphyrias, the major biochemical abnormalities occur in the red cell series. These include the rare congenital photosensitive porphyria (Gunther’s disease) and erythropoietic protoporphyria. The latter is a very interesting, recently discovered subvariant in which there is no abnormality of porphyrins in the urine but excessive levels of protoporphyrin in red cells and feces, associated with solar erythema or even eczema. Hepatic porphyria is more fre-

TABLE 2.—Classification of Porphyria

- (a) Erythropoietic porphyria
1. Congenital photosensitive (Gunther)
2. Erythropoietic protoporphyria (Magnus)
- (b) Hepatic porphyria
1. Acute intermittent (Swedish, pyrrolia)
2. Variegate (protocoprotoporphyria, South African)
3. Acquired—alcohol, hexachlorobenzene, tumor, etc.

### EXCRETION OF PORPHYRINS AND PRECURSORS



NORMAL					
URINE	1-2 mg.	1-2 mg.	10- 30x	100- 300x	0
FECES	0	0	0	400- 1000x	500- 1200x
ACUTE, INTERMITTENT PORPHYRIA					
URINE	+++ (15- 180mg.)	+++ (20- 200mg.)	+++	++	0
FECES	0	0	0	+	+

Chart 6.—Diagram showing the precursors glycine and succinate and the main pathway of porphyrin synthesis terminating in heme. ALA, delta aminolevulinic acid; PBG, porphobilinogen; uro, uroporphyrin; copro, coproporphyrin; proto, protoporphyrin.

quent. This includes acute intermittent porphyria, sometimes called the Swedish type, of which we have seen an example this morning. In addition, there are variegate porphyria, sometimes called South African porphyria or proto-coproporphyria. The acquired form of hepatic porphyria is that seen in alcoholism, in hexachlorobenzene poisoning and rarely with tumors. Although such cases are thought to be acquired, the possibility of genetic predisposition exists. Let us turn our attention to acute intermittent porphyria.

Acute intermittent porphyria (AIP) is a misnomer, as was noted previously, since the defect is presumably present from conception and the abnormalities could be most accurately called "pyrrolia." The disorder is transmitted as a dominant trait, with the onset of symptoms after puberty. The symptoms and signs may be acute and intermittent and may be precipitated by a variety of agents including barbiturates, alcohol, estrogens, griseofulvin and a number of other drugs. The clinical features of AIP are summarized in Table 3 and will not be discussed in detail here. It should be noted that recent studies have demonstrated inappropriate antidiuretic hormone secretion, with water intoxication, in a number of patients with this form of porphyria. I have seen a patient who was diagnosed as having Addison's disease because of abdominal pain and hyponatremia. The major clinical complications are neurological. Prognosis may be very serious with a mortality rate in Goldberg's series of approximately 24 per cent over a five-year period. This leaves us with two major questions. The first is, What is the basic metabolic defect in acute intermittent porphyria? The second and related question is, How does this metabolic defect produce the signs and symptoms of this disease?

The gross facts of the chemical changes found in acute intermittent porphyria are well known. Most characteristically, there is excessive excretion

of delta aminolevulinic acid and porphobilinogen. Secondly, there may be increased excretion of a variety of porphyrins, but it is thought that these may very likely occur as chemical artifacts formed because of the high reactivity of PBG. The difficulties which have arisen in defining the type of porphyrins excreted in acute intermittent porphyria may very well depend upon factors such as pH, ion concentration and other changes in the chemical environment which influence the type of porphyrin formed non-enzymatically from these precursors. These urinary porphyrins often appear as zinc complexes, but no abnormality of zinc metabolism has been detected. This is a disease of porphyrin precursors primarily, rather than of porphyrins. The metabolic defect seems to be localized to the liver. No abnormality has been found in red cells, and the elevated levels of porphyrin precursors are found predominantly in the liver and not in the marrow.

Why do excessive amounts of ALA and PBG accumulate? This must result from one of two possible causes. First, it might result from a decrease in the utilization of ALA or perhaps more likely of PBG. The accumulation of porphyrin precursors by this mechanism would be analogous to the accumulation of phenylalanine and its by-products in phenylketonuria. We can summarize research work carried out for over a decade, by saying that at present there is no good evidence for any block in heme synthesis in acute, intermittent porphyria. Furthermore, the levels of catalase in the liver are normal in this disorder. It has been postulated that the Shemin pathway may be blocked with subsequent accumulation of ALA, but this has not been demonstrated. As noted, most evidence has suggested that this pathway is quantitatively unimportant.

The second possibility is that there is overproduction of delta aminolevulinic acid as the primary defect. Once again this might result from one of two causes: there might be excessive amounts of substrates present—in this case glycine or succinyl Co-A—or there might be overactivity of the specific enzyme catalyzing the reaction, delta aminolevulinic acid synthetase. At present there is nothing to indicate a primary defect in glycine metabolism in porphyria. Diseases characterized by hyperglycinemia do not have porphyria, and the evidence suggesting a possible impairment of the incorporation of glycine into serine is not convincing. Furthermore, porphyrin

TABLE 3.—*Clinical Features of Acute Intermittent Porphyria*

- (a) Abdominal pain—spasm, nausea, vomiting
- (b) Neurological abnormalities—  
Peripheral neuropathy (particularly motor)  
cranial nerve palsies  
convulsions, coma
- (c) Psychic disturbances—anxiety to frank psychosis
- (d) Fever, leukocytosis
- (e) Inappropriate antidiuretic hormone secretion  
(hypotonicity)
- (f) Elevation of PBI without hypermetabolism



synthesis is quantitatively not a very important pathway of glycine metabolism, since the turnover of glycine in man is prodigious, perhaps 50 gm a day. Similarly, there is no evidence of an abnormality of succinyl Co-A metabolism as a primary defect. By a process of elimination, we must conclude that overactivity of the enzyme is the probable cause of oversynthesis of ALA. This concept finds support in the work of Grannick and Urata which has shown quite clearly that in experimental porphyria induced by the use of certain drugs, there are elevated levels of ALA synthetase in liver mitochondria.

Within the past few months, Tschudy and his colleagues<sup>2,3</sup> have found elevated levels of hepatic delta aminolevulinic acid synthetase in a single patient with acute, intermittent porphyria. The increase was about seven to fourteen-fold. This was reported in only one case, but we need not doubt that this will be confirmed in the disease. This brings us to the next question, Why is delta aminolevulinic acid synthetase elevated in a metabolic disease? No one knows, I think it is fair to say at present.

There are a number of variables in enzyme action. The amount of enzyme physically present may be under genetic control. The activity of the enzyme may also be genetically controlled. For example, its turnover rate or its affinity for the substrates might be altered in such a way that it is more active with the same concentration of enzyme. There may be a change in the response to control mechanisms, such that it is no longer subject to feedback inhibition. In this suggestion, acute intermittent porphyria might be an allosteric disease with loss of appropriate feedback inhibition, by which heme normally shuts off or dampens the synthesis of ALA as a controlling mechanism at the first stage of porphyrin biosynthesis. There are other possible defects in the genetic control of the amount of an enzyme present. There might be, for example, a defect in an operator gene such that it is no longer subject to repression by cytoplasmic repressor agents, so that the structural gene which codes the ALA synthetase might be constantly "turned on," resulting in excessive production of this protein. We do not know.

There is one major overriding fact that leads to the conclusion that porphyrin abnormalities may have very little to do with acute intermittent porphyria. In brief, there is nothing known phar-

macologically of these compounds, which have been studied over many years, to suggest that they are productive of the neuropathic changes or the abdominal symptoms that are characteristic of the disease. In fact, we must suspect that if porphyrins were colorless, the chemical relationship of ALA and porphobilinogen (PBG) to acute intermittent porphyria might never have been discovered. Is it possible that the exclusive attention directed to porphyrin biosynthesis in acute intermittent porphyria over the past 10 years may have even retarded our understanding of this important disease? Perhaps the porphyrin abnormalities, striking though they are, are merely an epiphenomenon of a more basic defect in the metabolism of nerve tissue. For example, there are abnormalities of tryptophane metabolism in phenylketonuria, a disease clearly shown to be due to a defect in the conversion of phenylalanine to tyrosine (phenylalanine hydroxylase). If exclusive attention had been directed to indolepyruvate and tryptophane metabolism, we would not now know the pathogenesis of phenylketonuria.

In summary, we can say that the known chemical abnormalities of acute intermittent porphyria can now be adequately explained by recent important work showing excessive levels of the specific rate-controlling enzyme in the porphyrin synthetic sequence. Nevertheless, the pathogenesis of the disease process, and of the elevated level of delta aminolevulinic acid synthetase, remains shrouded in biochemical mystery.

I am particularly glad that Dr. Welland from Stanford is here. He has worked with Dr. Tschudy and has been very active in this field. I hope he will comment on the pathogenesis of acute intermittent porphyria. Dr. Welland.

DR. FRED WELLAND:\* Thank you, Dr. Smith. First of all, a couple of comments about the patient. I suspect that you have an inkling that one of the parents has or had acute intermittent porphyria, even though it has been latent. In our experience with 10 or 15 sibships, a positive Watson-Schwartz test has always been found in a parent or a sibling. History of a mysterious death after an operation may suggest porphyria in a relative.

Secondly, the management of a porphyric patient of this type is most difficult. People with this

\*Chief Resident in Medicine, Stanford University.

disease are trying to live a normal life and yet they are sometimes disabled by terrible pain, and may become narcotic addicts. I might suggest the use of ganglionic blockers. Certainly when used intravenously in patients who are in hospital, these drugs have given fine relief for very short periods. Unfortunately, doses that must be given cannot be tolerated by an ambulatory patient because of postural symptoms.

Finally, I think you have appropriately emphasized, Dr. Smith, the really exciting problem in acute porphyria. This is a disease of the nervous system, and those of us who participated in the work with Dr. Tschudy on ALA synthetase are every bit as willing as you to admit that while we have this nice enzymatic finding which explains the urinary abnormality, we are no closer to understanding the pathogenesis of the disease. I personally remain hopeful that in fact we may have a unique opportunity for an inroad into the study of the biochemical mechanisms in nervous disease by the study of acute intermittent porphyria.

EDITOR'S NOTE: Over the past seven months, in the hospital, the patient has been treated with inosine, sodium bicarbonate, chlorpromazine and occasionally meperidine for abdominal pain. He has had several minor episodes of abdominal pain, only a few being associated with dark urine.

#### ACUTE INTERMITTENT PORPHYRIA

##### Recent Summaries in the Literature

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**California  
Medicine**

## EDITORIAL

### Plusses and Minuses

#### The California Medical Assistance Program

BECAUSE it may cast light on what to expect of the operation of the Federal "Medicare" program when it goes into effect 1 July, experience thus far with California's somewhat similar plan, which was begun 1 March of this year, is a matter of considerable interest to physicians the country over.

This comprehensive plan, called California Medical Assistance Program (CMAP), was passed by the 1965 Legislature "to pay for basic health care of eligible persons [the needy of various categories, including the aged indigent] . . . through a system of prepaid health care or contract with carriers." The State entered into a contract with California Physicians' Service and the California Blue Cross Plans to deal with claims under the program. More than 20 foundations for medical care have agreed with CPS to assist in reviewing physicians' claims.

The total number of potential eligibles under the program is estimated at about 2,500,000. A little less than half of that number is made up of persons who are on public assistance rolls, and the remainder comprises those who, although in the main self-supporting, might have to have help in event of need for extraordinary medical care.

During the first three months of the program, over 2,300,000 claims were received by the contractors from physicians, hospitals, nursing homes, home health agencies, rehabilitation centers, den-

tists, clinical laboratories, pharmacists, registered nurses, chiropractors, podiatrists, physical, occupational and speech therapists, optometrists, psychologists and those furnishing ambulance service, prosthetic devices, hearing aids and eyeglasses.

More than 105,000 claims have been received from hospitals, nursing homes and other institutions, and the amounts paid on those claims has reached about \$15,000,000. Drug claims led all the rest, numbering approximately one and a half million, on which \$1,240,000 has been paid. More than 350,000 physician claims have been received and \$4,500,000 has been paid on them.

Some claims have been returned for technical or administrative reasons such as insufficient information. Others have not been processed because the carrier cannot establish eligibility of the person treated. Some county welfare departments have experienced difficulty and delays in supplying up-to-date eligibility information that the CPS-Blue Cross administration must have to process claims.

Confusion among physicians and clinical laboratories has been caused by reduction of claims for clinical laboratory services. The reductions were made because the State Department of Finance imposed a maximum schedule of allowances on all clinical laboratory procedures, whether performed by a physician or in a licensed laboratory. The schedule adopted is based on the 1964 Relative Value Studies with unit values converted at a \$4 factor. Efforts to change this rule and this conversion factor have not yet been successful but they are still being pressed.

There have also been misunderstandings about allowances for medically necessary injections, immunization materials and other supplies furnished by the treating physician. On this point a clarifying letter of instruction has now been received by

the contractor, stating that "necessary drugs, materials and supplies *provided by the physician* may be charged for separately . . ."

In addition to the schedule of allowances for laboratory services, the State Department of Finance has published a maximum schedule of allowances for physical therapy, dental, chiropractic, podiatric and optometric services, as well as for hearing aids, eyeglasses and prosthetic and orthotic appliances. The State is at present developing fee schedules covering the services of psychologists, speech and hearing centers, ambulance services and the like. Hospitals and nursing homes are paid on the basis of certified cost statements submitted by them.

Over all, some 50 to 90 per cent of the claims received from various areas of the state for physicians' services are within the range of charges which might be expected, based on the experience of review committees and surveys that have been conducted by the CMA and county medical societies. For the most part claims within the expected range have been paid promptly. Other physicians' claims are being reviewed by local committees to determine if they are "reasonable" and within the range of customary or prevailing charges in the community as well as in accord with the usual charge by the physician for a comparable service for comparable patients. We are advised that in some instances the treating physician may have made a mistake in identifying the procedure

he performed, and that when this detail is reviewed and corrected the claim can be paid.

The review committees have also been scrutinizing utilization patterns. In this area of review the opinion of the medical community will be controlling and persuasive with the carrier and the courts. Such activities call for both objectivity and courage. We are sure that the medical review committees will equip themselves well with fact and sound judgment, and thus safeguard both the public and the profession.

Based on early reports, there is reason to congratulate the medical profession, in the main, for billing a reasonable charge for services rendered—one that is not higher than the charge for a comparable service generally made by the physician and is within the customary, current, prevailing range of charges in the locality for similar services.

A word of commendation is due also to the California Physicians' Service and Blue Cross plans for the efficient way in which they have administered this tremendous new program. As omissions and weaknesses have been located, they have been corrected with dispatch.

Likewise, the State administrators—Mr. Paul Ward, Dr. Lester Breslow (M.D.), Dr. Fernando Torgerson (Ph.D.), Mr. J. M. Wedemeyer and the others who have worked many long hours with them—have our approbation for the understanding and good will they have evidenced in implementing this program.





# California Medical Association



## NOTICES AND REPORTS

### ACTIONS OF THE HOUSE OF DELEGATES

Los Angeles, March 19 to 23, 1966

NOTE: *The following report of the transactions of the House of Delegates of the California Medical Association is selected and abridged. A complete transcript of all proceedings is on file in the Association office in San Francisco and available for the inspection of all members.*

#### REFERENCE COMMITTEES

COMMITTEES APPOINTED by Speaker William F. Quinn at the first meeting of the House of Delegates Saturday evening, March 19, were as follows:

*Committee on Credentials:* A. J. Murrieta, Jr., Los Angeles, chairman. A through L component societies: George C. Anderson, Hermosa Beach; George S. Buehler, Whittier; Thomas Elmendorf, Willows; Theodore S. Goldman, Beverly Hills and Paul D. Yates, Hermosa Beach.

M through Z component societies: Jack W. Baker, Temple City; J. Lafe Ludwig, Los Angeles; S. A. Skillicorn, San Jose; Helen B. Weyrauch, San Francisco and Harold E. Wilkins, Downey.

*Reference Committee 1.* (This committee reviews the reports of the officers, the Council, the commissions and standing and special committees.) Stanley Kirk, Paso Robles, chairman; John A. Bullis, Los Angeles; Paul C. Doehring, Glendale; Oscar W. Hills, San Mateo and Gerald Ingle, Corning.

*Reference Committee 2.* (This committee on finance reviews the reports of the secretary, executive secretary and studies and makes recom-

mendations to the House of Delegates on the budget submitted by the Council and the amount of dues for the ensuing year.) Carl E. Horn, Sacramento, chairman; Norman C. Fox, San Bruno; Ralph M. Milliken, Los Angeles; A. B. Sirbu, San Francisco and Chester Tancredi, San Diego.

*Reference Committee 3.* (This committee considers new and miscellaneous business.) Charles B. Hudson, Oakland, chairman; Robert L. Hippen, San Diego; Robert T. Hood, Jr., Van Nuys; Harold Miles, Santa Barbara and Horace F. Sharrocks, Sebastopol.

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*Reference Committee 3A.* (To consider business of Committee 3 when the volume becomes too great for one committee to handle.) William K. Hokr, San Diego, chairman; Leonard M. Asher, Beverly Hills; Dexter T. Ball, Santa Ana; M. M. Haskell, Long Beach and H. Dean Hoskins, Oakland.

*Reference Committee 3B.* (This committee also is a supplement to 3 and 3A.) Henry Gibbons, III, San Francisco, chairman. Edward Liston, Palo Alto; Daniel G. Morton, Los Angeles; Homer C. Pheasant, Los Angeles and J. B. Price, Santa Ana.

*Reference Committee 4.* (This committee considers amendments to the Constitution and By-laws.) Chester E. Herrod, San Francisco, chairman; Ralph D. Beasom, Los Angeles; Robert L. Day, Bakersfield; Mason Hohl, Beverly Hills and Ralph M. King, La Mesa.

*CPS Reference Committee:* (This committee considers new and miscellaneous business pertaining to the California Physicians' Service.) Edward J. Twigg, Oakland, chairman; Roger W. Barnes, Los Angeles; Robert C. Combs, San Francisco; J. E. Vaughan, Bakersfield and Francis E. West, San Diego.

#### PRESENTATION OF FIFTY-YEAR AWARDS

Pins commemorative of 50 years of membership in the California Medical Association have been presented to the following physicians: Alameda-Contra Costa: George E. Walton; Los Angeles County: John W. Crossan, Karl L. Die-

terle, Ernest C. Fishbaugh, Joseph Jacobs; Sacramento County: Nathan G. Hale, J. Roy Jones, Frank B. Reardan; San Diego: James F. Churchill; San Francisco: Orah K. Allen, Joseph Catton, Earl Greenwood; San Joaquin County: Elmer Smith; Santa Clara County: J. Samuel Staub.

#### RECOGNITION AND AWARDS

Ralph C. Teall was presented a plaque for his two years of dedicated service to the CMA as president-elect and as president. Newly elected President James C. MacLaggan received the president's gavel of the California Medical Association, as well as a gavel presented by the San Diego County Medical Society, which was handmade by 1st District Councilor, Roger C. Isenhour. Plaques for outstanding contributions were presented to the following: Matthew N. Hosmer, on his retirement as Secretary of the CMA after seven years of dedicated service; Llewellyn E. Wilson, retiring as CMA Councilor from the Second District; Mrs. Olive Neick, as outgoing chairman of the Medical Executives Conference; and Mr. Joseph F. Donovan, for twenty years of devoted service as executive secretary of the Santa Clara County Medical Society. W. D. Snively, Jr., and R. L. Westerman received the California Medical Education and Research Foundation "Aesculapius Award," sponsored by the Mead Johnson Laboratories, for their exhibit on "Clinical Potassium Deficit," judged the Best Scientific Exhibit of the 1966 Scientific Assembly.





# ACTION ON RESOLUTIONS

ONE HUNDRED EIGHT RESOLUTIONS came before the 1966 House of Delegates. Each was numbered and assigned to a Reference Committee for consideration and recommendation.

Reference Committees have the option of recommending a resolution for adoption or rejection, for adoption as amended or substituted, or for no action.

Resolutions shown here are in the form in which the House of Delegates approved them for adoption or for referral to the Council or to specified commissions or committees. Where a resolution was not adopted, that report is made here but the language of the resolution is not shown. Copies are available in the CMA office on request.

Each resolution is shown by number and subject and the name and status of each author is recorded. Where the House of Delegates action encompassed more than one resolution, notes give reference to all items covered by a single action.

## STANDARDIZATION OF HOSPITAL RECORDS

Resolution No. 1-66

Committee 3

Introduced by: Joseph W. Telford, M.D.

Representing: San Diego Delegation

WHEREAS, the California Medical Association Hospital Staff surveys have found that there are a multitude of different forms and methods used in compiling medical charts in the California Hospitals; and

WHEREAS, there is an obvious need for both standardization and simplification of the medical records; and

WHEREAS, all concerned with the use of medical records could benefit; and

WHEREAS, such standardized and simplified medical records will help facilitate the study of patient flow in hospitals; now, therefore, be it

**Resolved:** That the California Medical Association through its Commission on Hospital Affairs, study the feasibility of establishing standardized and simplified hospital records throughout the State of California; and be it further

**Resolved:** That the California Hospital Association be requested to cooperate in establishing such record forms should they prove feasible.

**ACTION:** Adopted by the House.

## IMPROVEMENTS OF SCIENTIFIC EXHIBITS

Resolution No. 2-66

Committee 3

Introduced by: Leon P. Fox, M.D.

Representing: Santa Clara County Medical Society

WHEREAS, the quantity and quality of scientific exhibits at the CMA annual sessions have not significantly improved over the years, usually being relegated to unattractive and inaccessible areas secondary to technical displays; and

WHEREAS, this tends to reflect an unjust, inferior image of the professional accomplishments of the CMA; and

WHEREAS, this has been a source of embarrassment and discouragement to exhibitors; and

WHEREAS, the Scientific Board has the responsibility of promoting educational improvement of our membership; now, therefore, be it

**Resolved:** That the Scientific Board be directed to re-evaluate and upgrade the quality and quantity of the annual scientific exhibit; and be it further

**Resolved:** That the pattern utilized by the AMA Scientific Board in the above be considered and that awards and other acknowledgments be inaugurated to attract high grade talent and expression.

**ACTION:** Adopted by the House.

## PROPRIETARY VISITING NURSES SERVICES

Resolution No. 3-66

Committee 3A

Introduced by: Marin Medical Society

**Resolved:** That the California Medical Association requests hearing of California Assembly Bill 19 at the earliest appropriate time.

**ACTION:** Above substitute resolution adopted by the House.

## SOCIAL SECURITY ADMINISTRATION PAYMENT FOR MEDICAL REPORTS

Resolution No. 4-66

Committee 3A

Introduced by: Tenth District

**Resolved:** That the California Medical Association recommend payment by governmental agencies for medical reports in accordance with prevailing patterns of payment for similar medical reports requested by non-governmental agencies and be it further

**Resolved:** That the CMA delegates to the AMA be instructed to press for similar action by the AMA House of Delegates at its next meeting.

**ACTION:** *Resolutions No. 4-66 and No. 37-66 were similar and considered together. The above resolution was adopted by the House as a substitute for No. 4-66 and No. 37-66.*

#### PHYSICIAN-HOSPITAL RELATIONSHIPS

Resolution No. 5-66

Committee 3A

Introduced by: Tenth District

[*Resolutions No. 5-66, 10-66, 18-66, 20-66, 38-66, 48-66, 49-66, 58-66, 63-66, 69-66, and 72-66 were considered at the same time because of their similarity. The below substitute resolution was offered in place of the aforementioned resolutions.*]

WHEREAS, historically there has been a conflict of opinion as to the proper relationship between hospital-based medical specialists and the hospitals; and

WHEREAS, Public Law No. 89-97 has brought into focus this historical conflict; and

WHEREAS, the American Medical Association House of Delegates, in special session in Chicago, October 1965, passed this policy:

"Hospital-based medical specialists are engaged in the practice of medicine. The fees for the services of such specialists should not be merged with hospital charges. The charges for the services of such specialists should be established, billed and collected by the medical specialists in the same manner as are the fees of other physicians;" and

WHEREAS, appointment of hospital-based medical physicians by the governing body should be only upon the recommendation of the medical staff, now, therefore, be it

**Resolved:** That the appointment of hospital-based physicians to medical staffs should be made in the same fashion as are all other staff physician appointments, and be it further

**Resolved:** That such physicians should not be denied staff appointment because of restrictive arrangements by the administration or the governing body of the hospital, and be it further

**Resolved:** That the agreement between hospital-based physicians and institutions must provide the optimum environment to assure the best service to patients and the medical staff and be subject to the continuing approval of the medical staff; and be it further

**Resolved:** That the policy of the California Medical Association conform to the policy of the American Medical Association as quoted above, and be it further

**Resolved:** That the California Hospital Association be notified of this resolution; and be it further

**Resolved:** That the California Medical Association, to implement this resolution, offer any possible assistance to component medical societies to help hospital medical staffs in their respective geographical areas during this period of transition.

**ACTION:** *Above substitute resolution amended as above and adopted by the House.*

#### BROADER DISSEMINATION OF HEALTH INFORMATION

Resolution No. 6-66

Committee 3

Introduced by: Leland B. Blanchard, M.D.

Representing: Scientific Board

WHEREAS, there is an increasing need for families to obtain authentic health information, to learn how to procure good medical care, to be better informed about the various types of health personnel, to learn the dangers of quackery and the indiscriminate use of drugs, and to become acquainted with the contributions organized medicine is making toward their health and welfare; and

WHEREAS, this information is contained in *Today's Health Guide* published by the AMA and available to anyone for a nominal cost; now, therefore, be it

**Resolved:** That the California Medical Association encourage all physicians in California to obtain a copy to become informed as to the contents of this guide and to suggest to them that they encourage families in their practice to likewise obtain a copy.

**ACTION:** *Adopted by the House.*

#### APPOINTMENT OF FAMILY PHYSICIANS TO MEDICAL SCHOOL FACULTIES

Resolution No. 7-66

Committee 3

Introduced by: Leland B. Blanchard, M.D.

Representing: Scientific Board

WHEREAS, there is a need for more family physicians; and

WHEREAS, several reasons for medical students not choosing family practice as a career result from the general absence of family physicians on medical school faculties; and

WHEREAS, most medical schools have written policy statements requiring physicians appointed to the faculty to be specialty board certified or eligible; and

WHEREAS, at least one school has appointed to the faculty family physicians without board certification to the mutual satisfaction of all concerned; now, therefore, be it

**Resolved:** That the California Medical Association encourage all medical schools in California



to appoint to their faculties an increasing number of family physicians with knowledge and skills to an appropriate degree in all fields of medicine and surgery.

**ACTION:** *Adopted by the House.*

### PARENT-CHILD RELATIONSHIPS

**Resolution No. 8-66** **Committee 3**  
Introduced by: Leland B. Blanchard, M.D.  
Representing: Scientific Board

WHEREAS, mental illness and juvenile delinquency are either the result of improper parent-child relationships or have this as one of the causes; and

WHEREAS, the degree of improper relationships in a family is related either to the degree of immaturity of the parents or their lack of knowledge of proper parent-child relationships or both; and

WHEREAS, the degree of immaturity of the offspring is related to the degree of improper parent-child relationships; therefore a vicious cycle is created by immaturity begetting immaturity; and

WHEREAS, the more immature the parents the less likely they are to seek information and assistance; and

WHEREAS, in our junior high and high schools there is a captive audience where an attempt can be made to educate future parents in proper parent-child relationships; now, therefore, be it

**Resolved:** That the California Medical Association encourage school administrators in California to attempt to teach junior high and high school students the importance and the principles of proper parent-child relationships.

**ACTION:** *Referred to Council for study.*

### GRADUATE TRAINING PROGRAMS IN FAMILY MEDICINE

**Resolution No. 9-66** **Committee 3**  
Introduced by: Leland B. Blanchard, M.D.  
Representing: Scientific Board

WHEREAS, with the continuing increase in medical knowledge and skills it is obvious that if consulting physicians are to encompass all of their field they must limit their practice to smaller and smaller segments of medicine or surgery; and

WHEREAS, with this fragmentation of the science of medicine there is an increasing need for family physicians to correlate this expanded medical care for the benefit of patients; and

WHEREAS, to meet the needs of the public for family physicians, more medical students must be encouraged to enter family practice; and

WHEREAS, one of the best methods to "sell" family practice to medical students is to allow them to witness it in operation; and

WHEREAS, a Board of Family Practice is in the process of being established which will make this field more attractive; and

WHEREAS, the number of training programs in family medicine for those graduates of medical schools who it is believed will be interested in family practice as a career, is seriously insufficient; now, therefore, be it

**Resolved:** That the California Medical Association in all possible ways lend its support to medical schools in this state for the enhancement of graduate training programs in family medicine already established or being designed and encourage them to originate such programs where none have been contemplated; and be it further

**Resolved:** That these graduate programs be based within the medical school affiliated hospital and be on a par with other graduate training programs.

**ACTION:** *Adopted by the House. Referred to Council for implementation.*

### HOSPITAL BASED SPECIALTIES CONTRACTS

**Resolution No. 10-66** **Committee 3A**  
Introduced by: Wallace A. Gerrie, M.D.  
Representing: Orange County Medical Association

**ACTION:** *See report on Resolution No. 5-66, with which Resolution No. 10-66 was combined.*

### MEDICAL INSURANCE FOR PEOPLE OVER 65

**Resolution No. 11-66** **Committee CPS**  
Introduced by: E. Kash Rose, M.D.  
Representing: Napa County Medical Society

[*This resolution was considered with Resolution No. 74-66.*]

**Resolved:** That CPS be encouraged to continue the development of programs for people over 65 years of age in the form of both complementary and substitute coverage to Medicare.

**ACTION:** *Above substitute resolution adopted.*

### OPPOSITION TO SENATE BILL 2568

**Resolution No. 12-66** **Committee 3B**  
Introduced by: Walter Carpenter, M.D.  
Representing: San Diego Delegation

WHEREAS, Senate Bill 2568 introduced in the U.S. Senate proposes to make it illegal for a physician to dispense drugs, devices, or eye-glasses to his patients; and

WHEREAS, the State of California Business and Professional Code specifically states that drugs, devices and eye-glasses may be dispensed by a licensed physician; and

WHEREAS, it is the opinion of the San Diego County Medical Society that any Federal Legislation concerning the dispensing of drugs, devices or eye-glasses patently infringes upon the privilege of the California licensing authority; and

WHEREAS, it is frequently in the best interest of patients to be able to obtain drugs, devices or eye-glasses from the attending physician, especially if the physician is in a remote area; now, therefore, be it

**Resolved:** That the California Medical Association go on record as opposing Senate Bill 2568 and take whatever action it deems necessary to assist in the defeat of this ill-advised legislation.

**ACTION:** *Adopted by the House.*

‘ ‘ ‘

#### REPORTING OF VENEREAL DISEASE

Resolution No. 13-66

Committee 3

Introduced by: Horace F. Sharrocks, M.D.

WHEREAS, the alarming increase in venereal disease incidence among teenagers and young adults has made V.D. California's most common communicable disease; now, therefore, be it

**Resolved:** That physicians be reminded that reporting of cases and permitting confidential interviews of patients by public health personnel are essential in the control of venereal disease. Performance of these services, as well as being required by law, is the physician's duty and responsibility.

**ACTION:** *Adopted by the House.*

**RECOMMENDATION:** *That this information be published in the publications of the CMA and other communication media of the various medical societies and also made a part of the orientation meetings at the component society level.*

‘ ‘ ‘

#### TITLE XVIII OF PUBLIC LAW 89-97

Resolution No. 14-66

Committee 3A

*[Resolutions No. 54-66 and No. 87-66 were considered with Resolution No. 14-66 because of similarity. These were combined into the below substitute resolution.]*

Introduced by: John Rumsey, M.D.

Representing: San Diego Delegation

WHEREAS, there has been established under Title XVIII, Part B of Public Law 89-97 a fee of \$6 per month, one-half coming from government sources; and

WHEREAS, Title XVIII, Part B lists a specific group of services to be covered by this sum; and

WHEREAS, both the State of California and the federal government have been expending large sums of money to induce eligible persons to participate in this program by extolling the potential benefits; and

WHEREAS, any fiscal failure of this program may possibly be blamed on physicians and hospitals rather than on the originating governmental agencies; now, therefore, be it

**Resolved:** That the California Medical Association expresses deep concern over the fact that the American people are expecting from Title XVIII, Part B, more than they have a reason to expect from a fiscal standpoint and they should be so notified; and be it further

**Resolved:** That the eligible beneficiaries should be clearly informed as to the limitations of this program by the responsible fiscal intermediaries.

**ACTION:** *Substitute resolution amended as above and adopted by the House.*

‘ ‘ ‘

#### RECLASSIFICATION OF MARIJUANA

Resolution No. 15-66

Committee 3B

Introduced by: San Francisco Delegation

*[Resolution No. 15-66 was combined with Resolution No. 16-66.]*

WHEREAS, Marijuana is now classified as a narcotic drug, and

WHEREAS, there is a great body of evidence to justify the classification of Marijuana as a dangerous drug producing habituation but not addiction, and

WHEREAS, the penalties for the unauthorized sale, manufacture, and possession of dangerous drugs are not the same as the penalties for the unauthorized sale, manufacture and possession of narcotic drugs; now, therefore, be it

**Resolved:** That the CMA urge the State Legislature to reclassify Marijuana from "Narcotic Drug" to "Dangerous Drug" and that the CMA study narcotics and dangerous drugs for the purpose of revision of present laws and their enforcement where advisable.

**ACTION:** *Above substitute resolution referred to Council.*

‘ ‘ ‘

#### NARCOTICS STUDY

Resolution No. 16-66

Committee 3B

Introduced by: San Francisco Delegation

*[See report on Resolution No. 15-66.]*



## Resolution No. 17-66

Committee 3B

Introduced by: San Francisco Delegation

[See report on Resolution No. 43-66 with which this resolution was combined.]

## PATHOLOGISTS—SERVICES

## Resolution No. 18-66

Committee 3A

Introduced by: San Francisco Delegation

**ACTION:** See report on Resolution No. 5-66, with which Resolution No. 18-66 was combined.

## UTILIZATION OF PARAMEDICAL PERSONNEL

## Resolution No. 19-66

Committee 3B

Introduced by: San Francisco Delegation

WHEREAS, there is increasing need for the most efficient utilization of paramedical personnel to provide basic medical care under the provisions of newly enacted law; and

WHEREAS, certain paramedical personnel can be trained to perform simple procedures such as giving injections and withdrawing blood samples from patients under the supervision of physicians; and

WHEREAS, such training can be included in the required education program of both LVN's and medical assistants with the provision of special training for talented candidates for the specialized function of withdrawing blood samples for laboratory analysis; now, therefore, be it

**Resolved:** That the CMA recommend changes in the Business and Professions Code to permit specially qualified and specially trained medical assistants and LVN's to give injections and to withdraw blood under stipulated conditions of supervision.

**ACTION:** Referred to the Liaison Committee to the Medical Assistants Association and the Committee on Other Professions. (At its 7 May meeting the Council referred this resolution to the Commission on Allied Health Professions and Services.)

PAYMENT OF SERVICES RENDERED  
BY RADIOLOGISTS

## Resolution No. 20-66

Committee 3A

Introduced by: San Joaquin County Delegation

Representing: San Joaquin County Medical Society

**ACTION:** See report on Resolution No. 5-66 with which Resolution No. 20-66 was combined.

## ETHICS REVIEW FOR COMPONENT SOCIETIES

## Resolution No. 21-66

Committee 4

Introduced by: Santa Barbara County Medical Society

**ACTION:** Because a quorum was not present this resolution was not considered by the House.

## Resolution No. 22-66

Committee 3

Introduced by: Council

WHEREAS, Malcolm H. Merrill, M.D., M.P.H., served the people of California for twenty-two years in furthering the "public health"; and

WHEREAS, Doctor Merrill made distinguished contributions as Director, State Department of Public Health; and

WHEREAS, the close cooperation and liaison between the California Medical Association and the State Department of Public Health was an integral part of his efforts; and

WHEREAS, the Council, by unanimous vote, has requested that the House of Delegates confer "Honorary Membership" in the Association on Doctor Merrill as specified in Chapter II, Section 4(b) of the Bylaws; now, therefore, be it

**Resolved:** That this House of Delegates elect Malcolm H. Merrill, M.D., M.P.H., an Honorary Member of the California Medical Association.

**ACTION:** Adopted by the House.

MILITARY DEPENDENTS  
MEDICAL CARE PROGRAM

## Resolution No. 23-66

Committee 3A

Introduced by: James O. Farley, M.D.

Representing: Sacramento County Medical Society

[Resolutions No. 23-66, No. 25-66 and No. 52-66 were considered together. The following substitute resolution was offered in their stead.]

WHEREAS, the military dependents medical care program remains largely based on the 1957 edition of the CMA Relative Value Studies at inadequate conversion factors despite the earnest and concerted efforts over many years of the CMA Committee on Federal Medical Care Programs to update fees; and

WHEREAS, the principle of the "usual and customary fee" has been established by Public Law 89-97; now, therefore, be it

**Resolved:** That the principle of the "usual and customary" fee should be used for the military dependents medical care program; and be it further

**Resolved:** That the California delegation to the American Medical Association present this resolution at the next meeting of the American Medical Association for its consideration.

**ACTION:** Above substitute resolution adopted by the House.

## USE OF DRAFTED DOCTORS

Resolution No. 24-66

Committee 3

Introduced by: ACCMA Delegation

WHEREAS, in the past in testimony before the Armed Services Committee of the House and Senate the American Medical Association has supported the "Doctors Draft" section of the Selective Service legislation as the only method of obtaining an adequate number of physicians for the Armed Forces; and

WHEREAS, many physicians each year under the threat of being drafted volunteer for the United States Public Health Service and thereby receive credit for the "draft obligation" while doing research work in the United States Public Health Service laboratories and other non-military duties; now, therefore be it

**Resolved:** That the American Medical Association be urged to support only such Selective Service legislation that will grant credit for fulfillment of draft obligation only to those physicians who become members of the Armed Forces.

**ACTION:** Amended as above and adopted by the House.

1 1 1

## USUAL AND CUSTOMARY FEES FROM ARMED FORCES MEDICARE

Resolution No. 25-66

Committee 3A

Introduced by: ACCMA Delegation

**ACTION:** See report on Resolution No. 23-66, with which Resolution No. 25-66 was combined.

1 1 1

## DRAFTING OF RESIDENTS

Resolution No. 26-66

Committee 3

Introduced by: ACCMA Delegation

**Resolved:** That the California Medical Association be asked to request the Selective Service System to provide at least six months notice to residents who are to be drafted and to the institutions in which they are engaged in residency; and be it further

**Resolved:** That Selective Service be asked to draft residents only at the completion of each year of their residency commitment.

**ACTION:** Adopted by the House.

1 1 1

## WORKMEN'S COMPENSATION

Resolution No. 27-66

Committee 3A

Introduced by: ACCMA Delegation

WHEREAS, health insurance policies now exclude coverage for patients with work-connected illnesses and injuries; and

WHEREAS, these patients are consequently seg-

regated into separate channels of medical care under the workmen's compensation medical care program; and

WHEREAS, such patients should be in the mainstream of medical practice, and should be entitled to receive care by the same physicians who provide their other health services; and

WHEREAS, in some cases it is difficult or impossible to determine whether a patient's illness is industrial or non-industrial, or to what degree it is industrial, and this results in confusion about whether the patient's case is covered by his health insurance, by workmen's compensation insurance, or partially by both; and

WHEREAS, the medical care of patients should not be fragmented into industrial and non-industrial portions, each treated by different physicians under different rules and different conditions; now, therefore be it

**Resolved:** That the California Medical Association urges:

1. Elimination of health insurance exclusions for work-connected illnesses and injuries, thus permitting coverage of these disorders by health insurance;

2. Payment by workmen's compensation insurance to health insurance carriers to reimburse them for their costs in covering industrial disorders; and

3. Use of workmen's compensation insurance in industrial cases to cover deductibles, co-insurance, and other medical costs that are not covered by the patient's health insurance.

**ACTION:** Referred to Council ad hoc Committee on Workmen's Compensation for study.

1 1 1

## INDUSTRIAL MEDICINE USUAL AND CUSTOMARY FEES

Resolution No. 28-66

Committee 3A

Introduced by: ACCMA Delegation

**ACTION:** No action was taken on this resolution because of its similarity with Resolution No. 101-66.

1 1 1

## CORONER FUNCTIONS

Resolution No. 29-66

Committee 3B

Introduced by: ACCMA Delegation

**Resolved:** That the California Medical Association House of Delegates endorses the concept that medical-legal investigation of deaths should be directly under the administration and jurisdiction of a physician, preferably a pathologist, whether these officials be titled coroners or medical examiners.

**ACTION:** Amended as above and adopted by the House.



## EXTENSION OF McATEER BILL

Resolution No. 30-66

Committee 3B

Introduced by: ACCMA Delegation

WHEREAS, the McAteer Bill providing for a comprehensive program for control of alcoholism is authorized to start 1 July 1966 and will terminate on 1 March 1967; and

WHEREAS, it is unreasonable to expect to recruit adequate staff, or to accomplish significant results in a program authorized for such a short period of time; now, therefore, be it

**Resolved:** That the California Medical Association House of Delegates expresses to the Legislature its recommendation that the program be continued for a minimum of three years.

**ACTION:** Adopted by the House.

‘ ‘ ‘

## INDEMNIFICATION FOR CLOSED PANEL PATIENTS

Resolution No. 31-66

Committee 3A

Introduced by: ACCMA Delegation

**Resolved:** That the California Medical Association House of Delegates recommends to all prepayment closed panel plans in California that they indemnify any of their patients who elect during an illness to obtain their medical care from a private physician.

**ACTION:** Adopted by the House.

‘ ‘ ‘

## DEPARTMENT OF MOTOR VEHICLES QUESTIONNAIRES

Resolution No. 32-66

Committee 3B

Introduced by: ACCMA Delegation

**Resolved:** That the Department of Motor Vehicles be asked to remove from its questionnaires questions which ask the doctor to make a judgment as to the patient's ability to drive and to confine its questions to those of a medical nature.

**ACTION:** Adopted by the House.

‘ ‘ ‘

## AMENDMENT TO PUBLIC LAW 89-97

Resolution No. 33-66

Committee 3A

Introduced by: ACCMA Delegation

**Resolved:** That the California Medical Association urges that the definition of "Post-Hospital Extended Care Services" in Section 1861 (i) of Public Law 89-97 be amended to delete the requirement that a patient be hospitalized for three days in a general hospital before he is eligible for nursing home care as defined in this section.

**ACTION:** Adopted by the House.

## AMENDMENT TO PUBLIC LAW 89-97

Resolution No. 34-66

Committee 3A

Introduced by: ACCMA Delegation

[Because of similarity this resolution considered with Resolution No. 46-66.]

WHEREAS, it will be a hardship upon some patients to ask them to pay their bills in full before reimbursement for medical care will be made by the fiscal intermediary under Part B, Title XVIII, Public Law 89-97; now, therefore, be it

**Resolved:** That the California Medical Association urge amendment to Public Law 89-97 to change that portion of part (ii)(B)(3)(b) of Section 1842 which now reads "such payment will be made on the basis of a receipted bill" to read "on the basis of a physician's bill."

**ACTION:** Above substitute resolution adopted by the House.

‘ ‘ ‘

## CALIFORNIA PHYSICIANS' SERVICE PAYMENTS

Resolution No. 35-66

Committee CPS

Introduced by: ACCMA Delegation

**Resolved:** That the California Medical Association request California Physicians' Service to implement Resolution 65-65 adopted by the 1965 CMA House of Delegates, which ordered identical CPS payments to all physicians for identical services in or out of the hospital in all those contracts which do not pay usual and customary fees.

**ACTION:** Referred to CPS Board of Trustees.

‘ ‘ ‘

## INDUSTRIAL MEDICINE—FREE CHOICE OF PHYSICIAN

Resolution No. 36-66

Committee 3A

Introduced by: ACCMA Delegation

**ACTION:** No action was taken on this resolution because of its similarity with Resolution No. 101-66.

‘ ‘ ‘

## PAYMENT BY GOVERNMENT AGENCIES FOR MEDICAL REPORTS

Resolution No. 37-66

Committee 3A

Introduced by: ACCMA Delegation

**ACTION:** See report on Resolution No. 4-66.

‘ ‘ ‘

## PAYMENT OF SERVICES RENDERED BY PATHOLOGISTS

Resolution No. 38-66

Committee 3A

Introduced by: San Joaquin County Medical Society

**ACTION:** See report on Resolution No. 5-66, with which Resolution No. 38-66 was combined.

## SEGREGATION IN COMPONENT SOCIETIES

Resolution No. 39-66

Committee 3

Introduced by: Marin Medical Society

WHEREAS, the California Medical Association has repeatedly stated that race, creed or color has no place in the criteria for membership in a medical organization; and

WHEREAS, beginning in 1939, resolutions were proposed to the American Medical Association from the Medical Society of the State of New York stating "That membership in component societies shall not be denied on the basis of race, creed or color"; now therefore, be it

**Resolved:** That the California Medical Association instruct its representatives to the American Medical Association to implement the introduction of the following amendment to the Constitution and Bylaws of the American Medical Association at the annual meeting to be held 26 to 30 June 1966:

"Membership in the American Medical Association of any constituent association shall be removed if such constituent association shall allow any component society to deny membership to any individual on the basis of race, creed or color."

**ACTION:** Above substitute resolution adopted by the House. Referred to the AMA Delegation.

**RECOMMENDATION:** That California Delegation to AMA attempt to join with other states so that states may introduce a joint resolution.

## CMA CANDIDATES FORUM

Resolution No. 40-66

Committee 3

Introduced by: Marin Medical Society

WHEREAS, the accuracy with which the American Medical Association reflects the thoughts of the American medical profession is dependent upon the accuracy with which physicians select their representatives to the AMA; and

WHEREAS, the selection of representatives should be, insofar as possible, on merit alone; and

WHEREAS, the more enlightened the electorate with regard to the merits of candidates, the more intelligent can be its choice; now, therefore, be it

**Resolved:** That, as a regular function of each annual meeting of the CMA, a forum be arranged at which each candidate for office of AMA delegate or alternate delegate make a statement regarding his qualifications for office and submit to a limited period of questioning regarding his views on current issues of importance to medicine.

**ACTION:** Adopted by the House and referred to Council for study.

## POLLUTION CONTROL

Resolution No. 41-66

Committee 3

Introduced by: Marin Medical Society

WHEREAS, environmental resources of land, water and air are not unlimited, and pollution of our environment is a significant and an ever-increasing problem; and

WHEREAS, the medical profession recognizes a responsibility, not only to the individually ill, but also to society generally; and

WHEREAS, doctors, by reason of their scientific training and long tradition of public service, are uniquely qualified to engage in pollution control endeavors; now, therefore, be it

**Resolved:** That the CMA continue, and even increase, its leadership in areas of environmental health and, furthermore, encourage and assist the county societies to participate, through their appropriate committees, in the study of local pollution problems, through the education of their members and the public, and making their position known to the responsible agencies, so that the best interests of environmental health and society are upheld.

**ACTION:** Adopted by the House.

## RESPONSIBLE HEALTH CARE FOR ALL

Resolution No. 42-66

Committee 3A

Introduced by: Marin Medical Society

**Resolved:** That the California Medical Association study in depth the feasibility of developing a program for medical care for individuals of all ages, utilizing the voluntary prepayment mechanism of the private insurance industry with financial support from government to the needy on a sliding scale for premium payment.

**ACTION:** Adopted above substitute Resolution and referred to Council for further study.

## ABORTION

Resolution No. 43-66

Committee 3B

Introduced by: Marin Medical Society

[This resolution was combined with Resolution No. 17-66.]

WHEREAS, resolutions were adopted in 1962 and 1963 (30-62, 37-62, 94-63) supporting the concept of medically justifiable abortion in this state; now, therefore, be it

**Resolved:** That this House reaffirm its position and express to the State Legislature its belief in the broadening of the therapeutic abortion law, taking into consideration the health of both the mother and the product of conception; and be it further



**Resolved:** That such legislation should provide proper medical control through established hospital staffs or component medical society committees.

**ACTION:** Above substitute resolution adopted by the House.

#### CALIFORNIA PHYSICIANS' SERVICE

Resolution No. 44-66 Committee CPS

Introduced by: Kern County Medical Society

[Because a quorum was not present, this resolution was not considered.]

#### CALIFORNIA PHYSICIANS' SERVICE

Resolution No. 45-66 Committee CPS

Introduced by: Kern County Medical Society

WHEREAS, the Foundations for Medical Care have been established by many Medical Societies in California; and

WHEREAS, the Foundations for Medical Care were organized for the purpose of reaffirming the faith of the general public in voluntary health insurance; and

WHEREAS, the Foundations for Medical Care have established standards for health insurance which meet the present day cost of medical care thereby allowing the public to adequately budget on a monthly basis for their medical needs; and

WHEREAS, the Foundations for Medical Care have met with excellent success not only in upgrading those sponsored insurance plans but also as the standard for all insurance written in a given community; and

WHEREAS, Foundations for Medical Care have demonstrated this value to the Public, the insurance carriers, and the physicians; now, therefore, be it

**Resolved:** That California Physicians' Service continue to utilize the Foundations for Medical Care to the fullest extent in implementing Title XVIII, Section B of Public Law 89-97 and Title XIX, known as AB-5 in California.

**ACTION:** Above resolution adopted as amended.

#### MEDICARE PAYMENT TO PATIENT

Resolution No. 46-66 Committee 3A

Introduced by: Howard W. Lindsey, M.D.

Representing: San Mateo County Medical Society

**ACTION:** See report on Resolution No. 34-66.

#### HOSPITAL BOARD MEMBERS

Resolution No. 47-66 Committee 3B

Introduced by: San Mateo County Delegation

Representing: San Mateo County Medical Society

WHEREAS, recent legislation and rapidly changing social and economic factors no longer permit the physician to remain aloof from the active supervision of the hospital in which he practices; and

WHEREAS, a voting interest in hospital affairs is essential to full expression of the physician's obligation cannot be satisfied by the non-voting representation of Chief of Staff and the Administrator; and

WHEREAS, the Board of Directors is unable to meet its full obligation to the interests of the medical community, including both the patients and the physicians, in the absence of a physician as a voting member of the Board; and

WHEREAS, the experience and training of a physician represent eminent qualifications for membership on the Board of Directors of a hospital; now, therefore, be it

**Resolved:** That the California Medical Association vigorously resist any legislation that would prohibit physician-membership on the Governing Board of a hospital; and be it further

**Resolved:** That the California Medical Association consider it highly desirable that physicians be members of the Governing Boards of hospitals.

**ACTION:** Amended as above and adopted by the House.

#### SEPARATE BILLING BY RADIOLOGISTS

Resolution No. 48-66 Committee 3A

Introduced by: C. Gerald Scarborough, M.D.

Representing: Santa Clara County

**ACTION:** See report on Resolution No. 5-66, with which Resolution No. 48-66 was combined.

#### DIRECT BILLING FOR PROFESSIONAL SERVICES

Resolution No. 49-66 Committee 3A

Introduced by: San Diego County Medical Society

**ACTION:** See report on Resolution No. 5-66, with which Resolution No. 49-66 was combined.

#### MEDICAL SELF-HELP IN SCHOOLS

Resolution No. 50-66 Committee 3

Introduced by: Frederick W. Ackerman, M.D.

Representing: ACCMA

**Resolved:** That the California Medical Association recommend to the State Board of Education that a course in medical self-help, on the level currently being offered by many local California medical association disaster medical care committees, be incorporated into the health education curriculum of all California secondary schools.

**ACTION:** Referred to Council for study.

## MOTORCYCLE SAFETY

Resolution No. 51-66

Committee 3B

Introduced by: Laurance A. Mosier, M.D.

Representing: Orange County Medical Association

WHEREAS, there is a rapidly growing number of available motorcycles and a growing number of motorcycle riders on our streets and highways; and

WHEREAS, there is an alarming increase in serious automotive accidents involving motorcycles; and

WHEREAS, it is possible under present California law to operate a motorcycle without prior experience and without the proven ability to ride a motorcycle safely; and

WHEREAS, at least five states in the United States now require special operators' licenses for motorcycles; and

WHEREAS, the Committee on Automotive and Traffic Safety in the California Medical Association has spotlighted the need for safety protection for motorcycle riders and has advised the use of helmets; now, therefore, be it

**Resolved:** That the California Medical Association use its influence in promoting state legislation to require special licenses for motorcycle operators subject to satisfactory completion of a motorcycle driving test; and be it further

**Resolved:** That the California Medical Association continue its efforts to encourage all motorcycle and motorbike operators to use the proper protective clothing, including a helmet.

**ACTION:** Adopted by the House.

‘ ‘ ‘

## ARMED FORCES DEPENDENTS MEDICARE

Resolution No. 52-66

Committee 3A

Introduced by: San Francisco Delegation

**ACTION:** See report on Resolution No. 23-66, with which Resolution No. 52-66 was combined.

‘ ‘ ‘

## AD HOC COMMITTEE ON STATE FEE SCHEDULES

Resolution No. 53-66

Committee 3A

Introduced by: San Francisco Delegation

**ACTION:** Resolution withdrawn by sponsors.

‘ ‘ ‘

## PUBLIC INFORMATION

Resolution No. 54-66

Committee 3A

Introduced by: San Francisco Delegation

**ACTION:** See report on Resolution No. 14-66, with which Resolution No. 54-66 was combined.

## GOVERNMENT HOSPITAL UTILIZATION COMMITTEES

Resolution No. 55-66

Committee 3A

Introduced by: San Francisco Delegation

WHEREAS, under recently enacted legislation, utilization committees are required for participation by accredited hospitals; and

WHEREAS, such utilization committees are being established in community voluntary and proprietary hospitals; and

WHEREAS, the accumulation of knowledge gathered by the utilization committees of the community is of such great value in the medical care of the community that no hospitals should be excluded from having utilization committees; and

WHEREAS, inclusion of government hospitals into the utilization review program might open up bed space in areas where there is a tremendous shortage of beds as well as serving the purpose of overall improvement of medical services; now, therefore, be it

**Resolved:** That the AMA be asked to bring to the attention of appropriate federal agencies the responsibility of government hospitals for establishing active utilization review committees.

**ACTION:** Above substitute resolution adopted by the House.

‘ ‘ ‘

## CHANNELING OF FUNDS

Resolution No. 56-66

Committee 3A

Introduced by: San Francisco Delegation

WHEREAS, Public Law 89-97 will draw a vast number of former clinic patients into the "mainstream" of medical care, and

WHEREAS, the government has stated its firm intent to pay reasonable charges; and

WHEREAS, there are several ways of channeling the funds obtained for the medical care of clinic patients; and

WHEREAS, each hospital medical staff might have varied opinions as to the proper, ethical disposal of these funds; now, therefore, be it

**Resolved:** That an appropriate committee of the CMA study the proper utilization of this potential income, in view of the existing governmental policy to pay physicians their usual and customary fee, and furnish this information to component medical societies.

**ACTION:** Above substitute resolution adopted by the House.



## VOLUNTARY ACCREDITATION OF HEALTH INSURANCE PLANS

Resolution No. 57-66

Committee 3A

Introduced by: San Francisco Delegation

**Resolved:** That the California Medical Association and the American Medical Association take immediate steps to join with such other interested groups as may seem appropriate to establish a "joint commission" or the like for voluntary accreditation of health insurance plans and other health benefit programs.

**ACTION:** *Adopted and referred with Resolution No. 64-66 to the AMA Delegation for introduction to the AMA House of Delegates.*

1 1 1

## DIRECT BILLING FOR PROFESSIONAL SERVICES

Resolution No. 58-66

Committee 3A

Introduced by: San Diego County Medical Society

**ACTION:** *See report on Resolution No. 5-66, with which Resolution No. 58-66 was combined.*

1 1 1

## NON-PARTICIPATION

Resolution No. 59-66

Committee 3A

Introduced by: Ralph Graham, M.D.

Representing: Orange County

**ACTION:** *Not adopted by the House.*

1 1 1

## CONTINUING MEDICAL EDUCATION

Resolution No. 60-66

Committee 3

Introduced by: Shasta-Trinity Medical Society

WHEREAS, it is generally accepted that continuing medical education is failing to reach a segment of the medical profession; and

WHEREAS, practically all physicians practice, at least some of the time, in hospitals; and

WHEREAS, medical schools and large metropolitan hospitals have gifted medical leaders and teachers; and

WHEREAS, these teachers in the main stream of advanced medical thought, could if subsidized, spend, on invitation of a hospital staff or department, days to weeks being active in lecturing, presenting wet and dry clinics, consulting, demonstrating, and shop-talking to the advantage of both the teachers and local physicians; now, therefore, be it

**Resolved:** That the House of Delegates recommend to the Committee on Continuing Medical Education that a study of the feasibility of this type of action be undertaken.

**ACTION:** *Adopted by the House.*

## PHYSICIAN PARTICIPATION IN LVN TRAINING

Resolution No. 61-66

Committee 3B

Introduced by: George D. Lavers, M.D.

Representing: Tulare County Medical Society

WHEREAS, there are an increasing number of LVN training programs in California; and

WHEREAS, the State Board of Vocational Nurse Examiners does not require physician participation in such training; and

WHEREAS, many LVN's coming from these programs know little of the physician's responsibility and role, so that they cannot immediately fit into the health team; now, therefore, be it

**Resolved:** That to insure the LVN graduate of wider knowledge concerning the practice of medicine and to facilitate her integration into the medical team, that the California Medical Association urge the State Board of Vocational Nurse Examiners to encourage physician participation in LVN training.

**ACTION:** *Adopted by the House.*

1 1 1

## MEDICAL DIAGNOSTIC PROCEDURES BY OPTOMETRISTS

Resolution No. 62-66

Committee 3

Introduced by: John A. Berg, M.D.

WHEREAS, increasing numbers of optometrists in California are procuring electric tonometric devices in an attempt to diagnose disease by measuring the intraocular tension of the eye without local ocular anesthesia; and

WHEREAS, such optometrists, encouraged by various optometric associations, are charging private patients for such medical diagnostic procedure on a fee for service basis and attempting to bill state and federal medical care programs for such procedure; and

WHEREAS, the Department of Professional and Vocational Standards' limitation on the scope of optometry does not include use of such medical diagnostic procedures and devices; now, therefore, be it

**Resolved:** That the CMA declare that ophthalmic tonometry is a specific medical diagnostic procedure and therefore is the practice of medicine.

**ACTION:** *Amended as above and adopted by the House.*

1 1 1

## SEPARATE BILLING FOR HOSPITAL RADIOLOGISTS

Resolution No. 63-66

Committee 3A

Introduced by: Robert E. Rousseau, M.D.

Representing: Santa Cruz County Medical Society

**ACTION:** *See report on Resolution No. 5-66, with which Resolution No. 63-66 was combined.*

## JOINT COMMISSION FOR ACCREDITATION OF VOLUNTARY HEALTH INSURANCE PLANS

Resolution No. 64-66

Committee 3A

Introduced by: Burt L. Davis, M.D.

Representing: Santa Clara

WHEREAS, many voluntary health insurance plans, both indemnity and service, are offered to the public; and

WHEREAS, patients frequently seek the advice of their personal physicians on matters pertaining to these coverages; and

WHEREAS, physicians cannot be conversant with the many details of this wide variety of contracts; and

WHEREAS, the CMA Medical Services Commission and the Bureau of Research and Planning have enumerated a number of criteria which should be met in any adequate form of health care coverage; and

WHEREAS, many of these policies are offered by companies incorporated in and doing their principal business in other states than California; and

WHEREAS, reputable insurance companies and the public have as great an interest in this subject as do physicians; now, therefore, be it

**Resolved:** That the Health Insurance Council, the National Association of Blue Shield Plans, the National Association of Blue Cross Plans, the Federation of Foundations, and other appropriate organizations be encouraged to join with the American Medical Association, the American Academy of General Practice, and the American Society of Internal Medicine, to form a Joint Commission for the Accreditation of Health Payment Plans which will operate to set standards, examine the extent of coverage, and investigate any other pertinent details of health plans; and be it further

**Resolved:** That upon the satisfaction of such requirements as may be deemed to be appropriate, to issue Certificates of Approval for those plans who voluntarily apply for same (the cost of operations to be met by appropriate application fees collected for such service); and be it further

**Resolved:** That the CMA delegates to the AMA introduce a resolution into the annual convention of the 1966 AMA House of Delegates for implementation of this concept.

**ACTION:** *Adopted and referred with Resolution No. 57-66 to AMA Delegation for introduction to the AMA House of Delegates.*

## USUAL, CUSTOMARY AND REASONABLE FEES

Resolution No. 65-66

Committee 3A

Introduced by: Roger Isenhour, M.D.

Representing: San Diego

WHEREAS, the Federal Department of Health, Education and Welfare and the Health and Welfare Agency of California have interpreted the "reasonable charges" in Public Law 89-97 and Assembly Bill 5 as consistent with the definition of "usual, customary and reasonable fees" as defined by Resolution 21 of the 1964 House of Delegates; and

WHEREAS, contrary to the legislative intent of Assembly Bill 5 and the established policy of the California Medical Association, the Department of Finance of the State of California has indicated an intent to establish a fixed schedule for laboratory services; and

WHEREAS, Public Law 89-97 and Assembly Bill 5 do not represent all of the medical practice covered by third party contracts; and

WHEREAS, the California Physicians' Service and the Foundations for Medical Care negotiate contracts involving physicians' fees; now, therefore, be it

**Resolved:** That the California Medical Association resist any effort by any governmental or other agency to establish fixed fees for physicians' services and procedures under the physician's supervision; and be it further

**Resolved:** That any organization associated with the California Medical Association, involved in discussions or negotiations of contracts involving doctors' fees, negotiate on the basis of the "usual, customary and reasonable fees," as defined by Resolution 21 of the 1964 House of Delegates.

**ACTION:** *Substitute resolution, amended as above and adopted by the House. (For definition of Resolution No. 21-64, see Resolution No. 81-66.)*

## STUDY COMMITTEES FOR INFANT AND MATERNAL HEALTH

Resolution No. 66-66

Committee 3

Introduced by: Leon P. Fox, M.D.

WHEREAS, the cooperative studies of the California Medical Association and the State of California Department of Public Health of maternal deaths since 1959, and of hemolytic disease of the newborn since 1963 have had great value in education of the profession, and improvement of patient care; and

WHEREAS, the continuation of the study of maternal deaths and the proposed study of infant deaths from infectious disease will have great additional value in the future; and

WHEREAS, educational aspects of these studies are now being greatly expanded both to the profession and to the public, and show great promise of further reducing maternal and infant mortality in the State of California; now, therefore, be it



**Resolved:** That the House of Delegates of the California Medical Association endorses the concept of these cooperative studies and goes on record as favoring that both the State of California and the California Medical Association continue budgets at present levels, pending Council & Finance Committee approval; and be it further

**Resolved:** That copies of this resolution be made available to the appropriate legislative committees and to the Public Health League.

**ACTION:** Amended as above and adopted by the House.

**CONDEMNATION OF CALIFORNIA BLUE CROSS AND WESTERN 65 INSURANCE CANCELLATION FOR MEDICARE RECIPIENTS**

Resolution No. 67-66 Committee 3A  
Introduced by: Los Angeles Delegation

**ACTION:** Tabled by the House.

**USUAL FEES A.B. 5**

Resolution No. 68-66 Committee 3A  
Introduced by: Los Angeles Delegation

WHEREAS, the California Medical Association has for years been seeking to establish the principle of reimbursement on a usual fee basis with due regard to regional variations for medical services rendered to patients whose medical care is being paid for by an agency of the State; and

WHEREAS, this principle has now been incorporated in the recently implemented California Medical Assistance Program (A.B. 5); now, therefore, be it

**Resolved:** That each doctor in California be urged to use his usual fee, together with the proper code number from the 1964 RVS in billing for his services; and be it further

**Resolved:** That each county medical society immediately implement adequate review committees to assist in the prompt adjudication of any claims requiring professional evaluation.

**ACTION:** Adopted by the House.

**HOSPITAL-PHYSICIAN CONTRACTUAL ARRANGEMENTS**

Resolution No. 69-66 Committee 3A  
Introduced by: Los Angeles Delegation

**ACTION:** See Report on Resolution No. 5-66, with which Resolution No. 69-66 was combined.

**SECTION 1801—PUBLIC LAW 89-97**

Resolution No. 70-66 Committee 3A  
Introduced by: Los Angeles Delegation

WHEREAS, P.L. 89-97 passed by the 1965 Ses-

sion of Congress contains many provisions which appear to permit the Department of Health, Education and Welfare to exert unusual interference and control over the manner in which Medicine is practiced in this country; and

WHEREAS, Section 1801—P.L. 89-97 was written to protect the public, the medical profession and hospitals from such interference and control; and

WHEREAS, the intent of Congress expressed in the various committee reports is very clear in that such interference and control is prohibited; and

WHEREAS, Representative Wilbur Mills, Secretary Gardner of HEW, Wilbur Cohen, Arthur Hess and other representatives of this Department have made many public commitments to honor this intent of the Congress; and

WHEREAS, a strict application of Section 1801 of the Law is the only guarantee medicine has against ultimate total Federal control of medical practice which was the basis of medicine's objection to this and other socialized medical laws; and

WHEREAS, the AMA House of Delegates in Philadelphia, November-December 1965, acknowledged the importance of a strict application of Section 1801—P.L. 89-97; now, therefore, be it

**Resolved:** That the California Medical Association House of Delegates affirms its policy to insist upon a literal interpretation of Section 1801—Public Law 89-97 in the implementation of this law.

**ACTION:** Adopted by the House.

**RESOLUTION OPPOSING SENATE BILL 2568**

Resolution No. 71-66 Committee 3B  
Introduced by: Los Angeles Delegation

**ACTION:** No action was taken on this resolution. See report on Resolution No. 12-66.

**FEES OF HOSPITAL-BASED MEDICAL SPECIALISTS**

Resolution No. 72-66 Committee 3A  
Introduced by: Los Angeles Delegation

**ACTION:** See report on Resolution No. 5-66, with which Resolution No. 72-66 was combined.

**INTER-AGENCY COUNCIL ON SMOKING AND HEALTH**

Resolution No. 73-66 Committee 3  
Introduced by: Los Angeles Delegation

WHEREAS, the activity of the Inter-Agency Council on Smoking is in the public interest; and

WHEREAS, this Inter-Agency Council welcomes active participation from organized medicine; now, therefore, be it

**Resolved:** That the California Medical Association take a more vigorous part in the activities of the Inter-Agency Council on smoking.

**ACTION:** Amended as above and adopted by the House.

#### CPS INSURANCE FOR PERSONS OVER AGE 65

Resolution No. 74-66

Committee CPS

Introduced by: Los Angeles Delegation

[See report on Resolution No. 11-66.]

#### TAX DEDUCTION FOR COLLEGE TUITION

Resolution No. 75-66

Committee 3B

Introduced by: Los Angeles Delegation

**ACTION:** No action taken by the House.

#### INSURANCE ASSIGNMENTS

Resolution No. 76-66

Committee 3A

Introduced by: Los Angeles Delegation

WHEREAS, the present Medicare Law (P.L. 89-97) states that an assignment of the fee to the doctor will represent the entire fee which the doctor can collect; and

WHEREAS, inability to charge a fee beyond that listed by the Medicare Program as the fee for a particular procedure, establishes a maximum fee therefor for the procedure no matter what the physician's fee might be (if he has accepted the assignment); and

WHEREAS, this represents interference in the physician's freedom of decision relative to fees; and

WHEREAS, this represents further interference with the free enterprise system of medical practice; now, therefore, be it

**Resolved:** That the present Medicare Law (P.L. 89-97) be changed so that the physician's fee is in no way limited by an assignment; and be it further

**Resolved:** That the California Medical Association take all necessary steps to implement this change.

**ACTION:** Adopted by the House.

#### DIRECT PATIENT BILLING

Resolution No. 77-66

Committee 3A

Introduced by: Los Angeles Delegation

WHEREAS, P.L. 89-97 provides that physicians may bill their patients directly for their services under both Title XVIII and Title XIX; and

WHEREAS, California Medical Assistance Plan

(A.B. 5-1965 California State Legislature Special Session) provides for this same right; now, therefore, be it

**Resolved:** That the California Medical Association inform all of its members of their rights under both Federal and State Law to bill all of their patients directly; and be it further

**Resolved:** That component societies of California Medical Association be urged to inform their members of the advantages and disadvantages of direct patient billing and the mechanism of billing for insurance intermediaries on an assignment basis.

**ACTION:** Referred to Council Task Force on Public Law 89-97.

#### CONSULTANTS TO AMA ADVISORY COMMITTEE TO THE DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

Resolution No. 78-66

Committee 3

Introduced by: Los Angeles Delegation

WHEREAS, Edward R. Annis, M.D., has been recognized as the most outstanding spokesman for American Medicine; and

WHEREAS, Edward R. Annis, M.D., was accorded special commendation as Medicine's spokesman by the AMA House of Delegates Interim Session in Philadelphia, December 1965; and

WHEREAS, Edward R. Annis, M.D., has a special knowledge from experience and in dealing with government; and

WHEREAS, Edward R. Annis, M.D., Amos N. Johnson, M.D., and William O. LaMotte, Jr., M.D., were designated as consultants to the AMA Advisory Committee to the Department of Health, Education and Welfare at the AMA Special Meeting in October 1965; and

WHEREAS, the intent of the policy established by the House of Delegates in 1965 was to include Edward R. Annis, M.D., Amos N. Johnson, M.D., and William O. LaMotte, Jr., M.D., at AMA Advisory Committee meetings; and

WHEREAS, these consultants have not been invited to attend these AMA Advisory Committee meetings; and

**Resolved:** That the California Medical Association recommends that Edward R. Annis, M.D., Amos N. Johnson, M.D., and William O. LaMotte, Jr., M.D., be used more fully by the AMA Advisory Committee to the Department of Health, Education and Welfare.

**ACTION:** Amended as above and adopted by the House.



## ROLE OF MEDICINE IN SOCIETY

Resolution No. 79-66

Committee 3B

Introduced by: Los Angeles Delegation

[*Because of similarity this resolution was considered with Resolution No. 98-66.*]

WHEREAS, a study of its own performance by a medical society, as a mechanism for critical self-evaluation, should serve as a vital force for the progress of organized medicine; and

WHEREAS, the study conducted by CMA and reported in the "Role of Medicine in Society" has identified many of medicine's problems; now, therefore, be it

**Resolved:** That the CMA House of Delegates accepts "The Role of Medicine in Society" as a report which in no way implies or reflects policy of the CMA; and be it further

**Resolved:** That the Council of the CMA continue the study of the "Role of Medicine in Society."

**ACTION:** *Above substitute resolution adopted by the House.*

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## PROPOSED RULES AND REGULATIONS

RE: P.L. 89-97

Resolution No. 80-66

Committee 3A

Introduced by: Los Angeles Delegation

WHEREAS, regulations for implementation of the Federal Public Law 89-97 have or will be published in *The Federal Register*; and

WHEREAS, all interested parties have 30 days to offer comments or objections to these regulations; and

WHEREAS, it is policy of the American Medical Association to offer such comment or objection as strongly as possible if proposed regulations threaten to interfere with medical practice or to endanger quality medical care and to encourage State and County Societies to likewise raise such objections; and

WHEREAS, Section 1801, P.L. 89-97 specifically prohibits interference of any Federal agency in the manner in which medical services are provided; now, therefore, be it

**Resolved:** That the appropriate California Medical Association Committee or Committees and committees of component societies immediately examine these proposed regulations and offer appropriate comment or objection to any regulation which directly or indirectly tries to exert control over medical practice or to interfere in the manner in which medical or hospital services are provided; and be it further

**Resolved:** That the members of the California

Medical Association and the public be made aware of these comments or objections.

**ACTION:** *Adopted by the House.*

~ ~ ~

## USUAL AND CUSTOMARY

Resolution No. 81-66

Committee 3A

Introduced by: Los Angeles Delegation

**Resolved:** That the California Medical Association House of Delegates affirms that the term "prevailing" conforms with the definition of "customary" as defined by Resolution 21 of the 1964 CMA House of Delegates.

**ACTION:** *Substitute resolution adopted by the House.*

NOTE: Resolution No. 21-64 defines as follows:

(a) Usual. The "usual" fee is that fee usually charged, for a given service, by an individual physician to his private patient (i.e., his own usual fee);

(b) Customary. A fee is "customary" when it is within the range of usual fees charged by physicians of similar training and experience, for the same service within the same specific and limited geographical area (socio-economic area of a metropolitan area or socio-economic area of a county);

(c) Reasonable. A fee is "reasonable" when it meets the above two criteria, or in the opinion of the responsible Medical Association's Review Committee, is justifiable, considering the special circumstances of the particular case in question.

~ ~ ~

## GOVERNMENT GRANTS

Resolution No. 82-66

Committee 3B

Introduced by: Los Angeles Delegation

**ACTION:** *Not adopted by the House.*

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## POISON PREVENTION

Resolution No. 83-66

Committee 3

Introduced by: Los Angeles Delegation

WHEREAS, each year an estimated half million children swallow medicines and household products which have the potential to cause serious injury and even death; and

WHEREAS, educational campaigns have proved effective in reducing the problem of accidental poisonings; and

WHEREAS, the Congress of the United States and the President have designated the third week in March as National Poison Prevention Week; and

WHEREAS, many nationally prominent organizations including the American Medical Association, the American Academy of Pediatrics, the Ameri-

can Association of Poison Control Centers, the American Hospital Association, the American Dental Association are cooperating in sponsoring Poison Prevention Week; now, therefore, be it

**Resolved:** That the House of Delegates of the California Medical Association herein convened does officially endorse the annual Poison Prevention Week in California; and be it further

**Resolved:** That each member of the California Medical Association become acquainted with the services available through the various Poison Information Centers in the State; and be it further

**Resolved:** That all members of the California Medical Association be urged to cooperate in Poison Prevention Week by disseminating all available educational material to their parents.

**ACTION:** Amended as above and adopted by the House.

#### MEDICAL LIBRARIES

Resolution No. 84-66 Committee 3B  
Introduced by: Los Angeles Delegation

WHEREAS, the Medical Library contributes directly to the health and welfare of the public; and

WHEREAS, taxation detracts from the contributions which the library can make to the welfare of the public; and

WHEREAS, such detractions from the health and welfare of the public is contrary to the public interest; now, therefore, be it

**Resolved:** That the California Medical Association Council and the Legislative Committee be requested to take all possible action to amend the law, to declare that medical libraries open to all members of the profession are public libraries and exempt from taxation.

**ACTION:** Adopted by the House. Referred to the Council and the Committee on Legislation for implementation.

#### RESOLUTION TO AMA RE: FUNCTION AND ACTIVITIES OF LEVELS OF ORGANIZED MEDICINE

Resolution No. 85-66 Committee 3  
Introduced by: Los Angeles Delegation

WHEREAS, the American Medical Association is contemplating a raise in dues; and

WHEREAS, the California Medical Association also is contemplating a raise in dues; and

WHEREAS, there are numerous programs being generated by the American Medical Association and the California Medical Association whose implementation will fall primarily on the County Medical Associations; and

WHEREAS, the specific areas of function, activity and influence of these various levels of our

medical organizations have never been specifically defined or integrated; and

WHEREAS, there has evolved through the years many areas of overlap of these functions, activities, and influence; now, therefore, be it

**Resolved:** That the California Medical Association House of Delegates herein assembled request their Delegation to the American Medical Association to submit a resolution to define and correlate these functions in the interest of effective organizational structure and economy.

**ACTION:** Amended as above and adopted by the House.

#### PHYSICIAN-HOSPITAL RELATIONSHIPS

Resolution No. 86-66 Committee 3  
Introduced by: Los Angeles Delegation

WHEREAS, there have been recent incidents where unilateral action has been taken by a hospital administration involving patient care and staff organization; and

WHEREAS, the *Guiding Principles for Physician-Hospital Relationships* established a method of cooperation between the medical staff and hospital administration where patient care and staff organization is involved; now, therefore, be it

**Resolved:** That the CMA reaffirm this section of the *Guiding Principles* and request the Joint Commission on Accreditation to review accreditation of hospitals where major decisions involving patient care and staff organization are made by unilateral decision of the hospital administration.

**ACTION:** Substitute resolution as above adopted by the House.

#### PUBLICITY FOR HEALTH CARE PLANS

Resolution No. 87-66 Committee 3A  
Introduced by: Los Angeles Delegation

**ACTION:** See report on Resolution No. 14-66, with which Resolution No. 87-66 was combined.

#### PUBLIC HEALTH LEAGUE

Resolution No. 88-66 Committee 3B  
Introduced by: Los Angeles Delegation

WHEREAS, the Public Health League of California has continuously since 1933 diligently and efficiently served the best interests of the California Medical Association in its relationships with the California Legislature; and

WHEREAS, the Public Health League of California has served in this same manner in concert with the Legislative Committee of the California Medical Association in fostering legislation reflecting the policies of the California Medical Association in affording the highest quality of medical care for all the state's citizens; and



WHEREAS, as a result of their efforts the California Medical Association has consistently enjoyed their efforts rewarded by the enactment of constructive legislation in the highest tradition of the medical profession; now, therefore, be it

**Resolved:** That the House of Delegates of the California Medical Association extend to the officers and staff of the Public Health League of California and to the Chairman and Members of the Committee on Legislation its sincere appreciation for an outstanding record of service and urge continued support by the entire membership of the California Medical Association of this effective legislative team.

**ACTION:** *Adopted by the House.*

#### GREATER COOPERATION BETWEEN THE MEDICAL AND LEGAL PROFESSIONS

Resolution No. 89-66 Committee 3  
Introduced by: Los Angeles Delegation

WHEREAS, there is a desire and need for greater cooperation between the medical and legal professions; and

WHEREAS, despite many laudable methods to assure this cooperation there still exists areas of dissatisfaction engendered by the threat of subpoena; and

WHEREAS, one of the main sources of dissatisfaction is engendered by asking a physician to retain time for purposes of a court appearance and then failure to notify the physician within a reasonable time that his presence is not needed; and

WHEREAS, this lack of notification results in a complete loss of services and recompense to the physician; now, therefore, be it

**Resolved:** That the California Medical Association go on record as endorsing the principle that when an attorney asks a doctor to retain time, said attorney should do so in writing and indicate who the responsible party is; and further be it

**Resolved:** That a physician has the right to charge a reasonable fee for his retained time, if he has not been notified that his presence was not needed at the previously indicated date in sufficient time to utilize that retained time.

**ACTION:** *Amended as above and adopted by the House.*

CHANGING NAME OF LEGISLATIVE COMMITTEE  
Resolution No. 90-66 Committee 3B  
Introduced by: Los Angeles Delegation

**ACTION:** *Not adopted by the House.*

TAX DEDUCTION FOR INSURANCE PREMIUMS  
Resolution No. 91-66 Committee 3B

Introduced by: Los Angeles Delegation

**ACTION:** *No action taken by the House.*

#### IMPLIED CONSENT LAW

Resolution No. 92-66 Committee 3B  
Introduced by: Los Angeles Delegation

**Resolved:** That the California Medical Association support and encourage the passage of legislation in California of the "implied consent" law, wherein automobile operators, by virtue of receiving licenses to operate automobiles in California, consent to the appropriate extraction of blood, under circumstances which create a suspicion that an automobile was operated under the influence of alcohol, for the determination of alcoholic content therein, and the use of the results of this chemical determination in court, both civil and criminal.

**ACTION:** *Above substitute resolution adopted by the House.*

#### GUIDING PRINCIPLES FOR PHYSICIAN-HOSPITAL RELATIONSHIPS

Resolution No. 93-66 Committee 3B  
Introduced by: Los Angeles Delegation

**Resolved:** That the Guiding Principles be amended on Page 9 to read as follows: "Upon each appointment to the medical staff, the physician shall subscribe, in writing, preferably in an appropriate space provided on the application form, to these Guiding Principles, or to the Constitution and Bylaws in which these Guiding Principles have been incorporated.

**ACTION:** *Above substitute resolution adopted by the House.*

#### BUREAU OF RESEARCH AND PLANNING

Resolution No. 94-66 Committee 3B  
Introduced by: Los Angeles Delegation

[*This resolution was considered with Resolution No. 95-66.*]

**ACTION:** *Not adopted by the House.*

#### BUREAU OF RESEARCH AND PLANNING

Resolution No. 95-66 Committee 3B  
Introduced by: Los Angeles Delegation

[*See report on Resolution No. 94-66.*]

#### AGENTS OF HEALTH CARE FINANCING PLANS

Resolution No. 96-66 Committee 3A  
Introduced by: Los Angeles Delegation

WHEREAS, Federal and State governments have entered into health care financing; and

WHEREAS, these programs are intended to cover all health care needs; and

WHEREAS, physician and hospital services can be judged solely on the medical necessities of the patient, and such judgment must of necessity be made by physicians; and

WHEREAS, limitation of finances does not change the medical necessities of the patient; and

WHEREAS, the physician who acts as agent or administrator of a health care financing plan who passes judgment on medical necessity of patient care has a conflict of interest; and

WHEREAS, Utilization Committees and Medical Review Committees do make such judgments; and

WHEREAS, Hospital staff committees are responsible solely to the hospital staff from which they originate; now, therefore, be it

**Resolved:** That the hospital medical staffs and their committees throughout California be reassured that their responsibility is solely to their respective staffs and not to governmental agencies or other outside organizations.

**ACTION:** Amended as above and adopted by the House.

1 1 1

#### THE ROLE OF MEDICINE IN SOCIETY

Resolution No. 98-66

Committee 3B

Introduced by: Frank A. Rogers, M.D.

Representing: Los Angeles

[See report on Resolution No. 79-66.]

1 1 1

#### MEDICARE APPLICATION QUESTION CONCERNING SUBVERSIVE ACTIVITIES

Resolution No. 99-66

Committee 3A

Introduced by: Leonard M. Asher, M.D.;

Douglas N. MacInnis, M.D.; Richard H. Mailman, M.D.

Representing: Los Angeles

**Resolved:** That the California Medical Association go on record as opposing any discriminatory law or regulation which might deny medical care to anyone otherwise eligible.

**ACTION:** Above substitute resolution adopted by the House.

1 1 1

#### COMMENDATION TO AMA-ERF

Resolution No. 100-66

Committee 3

Introduced by: Council

**Resolved:** That the California Medical Association reaffirm its positive support of AMA-ERF and the projects it sponsors by developing state and local AMA-ERF committees to assist the Board of Directors and the staff of AMA-ERF in their efforts to increase physician understanding and voluntary financial support for AMA-ERF projects.

**ACTION:** Adopted by the House.

#### FREE CHOICE OF PHYSICIAN

Resolution No. 101-66

Committee 3A

Introduced by: San Mateo Delegation

[Resolution No. 28-66, 36-66 and 102-66 were similar to Resolution No. 101-66.]

WHEREAS, the medical legislative trend, both state and national, is to recognize the concepts of free choice of physician by the patient and the usual, customary and reasonable fee; now, therefore, be it

**Resolved:** That the California Medical Association reaffirm its belief in these concepts and that the California Medical Association continue to strive toward these goals for all with particular respect to those whose care is currently provided for by the Workmen's Compensation Law and the Crippled Children's Services, and that the California Medical Association oppose that portion of any other or new categorical program which does not conform to these concepts.

**ACTION:** Adopted by the House.

1 1 1

#### WORKMEN'S COMPENSATION

Resolution No. 102-66

Committee 3A

Introduced by: San Mateo Delegation

**ACTION:** No action was taken on this resolution because of its similarity with Resolution No. 101-66.

1 1 1

#### WORKMEN'S COMPENSATION

Resolution No. 103-66

Committee 3A

Introduced by: San Mateo Delegation

**Resolved:** That if a Register of Physicians for Workmen's Compensation cases is authorized by the California Medical Association, that it be clearly and prominently stated on this Register that a physician's listing in this Register does not imply or require his acceptance of the Industrial Accident Commission Minimum Fee Schedule as full payment for services; and be it further

**Resolved:** That the California Medical Association inform the Industrial Accident Commission and the Workmen's Compensation insurance carriers that payment of usual and customary fees will result in the ready availability to the industrially injured of the services of essentially all practicing physicians in the California Medical Association.

**ACTION:** Above substitute resolution adopted by the House.



## PHYSICIAN'S COMPENSATION FOR ADMINISTRATIVE REQUIREMENTS

Resolution No. 104-66

Committee 3A

Introduced by: Frank J. Novak, M.D.

Representing: San Mateo County Medical Society

WHEREAS, the new government health programs require hospitals to have "Utilization Review" committees in order to be reimbursed by these government health programs; and

WHEREAS, only physicians can serve on hospital committees affecting medical care; now therefore, be it

**Resolved:** That physicians be compensated for servicing the administrative requirements of hospital utilization committees.

**ACTION:** *Referred to Committee on Hospital Affairs for further study.*

1 1 1

## MEDICAL LABORATORY STUDY

Resolution No. 105-66

Committee 3

Introduced by: Abe E. Berman, M.D.

Representing: Sacramento County Delegation

**Resolved:** That the California Medical Association invite the California Society of Pathologists and other interested groups to join in a study of current medical laboratory practices in California, including, but not limited to:

1. Non-medical directed laboratories;
2. Contiguous-state laboratory licensing regulations, advertising and solicitation practices;
3. Changes in present state licensing regulations to assure maintenance of high quality medical laboratory work in light of rapidly changing laboratory technology.

**ACTION:** *Amended as above and adopted by the House.*

## "CAL-MED"

Resolution No. 106-66

Committee 3A

Introduced by: Delegates from Los Angeles

**ACTION:** *Not adopted by the House.*

**RECOMMENDATION:** *That Council study the "CAL-MED" proposal in depth and make frequent reports to the members of the House.*

1 1 1

## ETHICAL PRACTICE OF ANESTHESIOLOGY

Resolution No. 107-66

Committee 4

Introduced by: Edward Twigg, M.D.

Representing: ACCMA

**ACTION:** *Due to lack of a quorum this resolution was not considered by the House.*

1 1 1

## COMMENDATION FOR SANTA BARBARA COUNTY PHYSICIANS

Resolution No. 108-66

Introduced by: Carl E. Anderson

Representing: Council

WHEREAS, the California Medical Assistance Program incorporates significant concepts relating to pre-payment; and

WHEREAS, for the past several years the Santa Barbara Plan provided a unique precedent in the application of pre-payment concepts to public assistance medical care; and

WHEREAS, this pilot program owes its outstanding success to the support of the physicians of Santa Barbara County and the sustained dedication of the County Society's review and quality of care committee, now therefore be it

**Resolved:** That this Council of CMA commend physicians of Santa Barbara County for the important contribution which they have made through the timely development and implementation of the Santa Barbara Plan which has proved so valuable in demonstrating the merits of private responsibility in pre-payment of government-financed programs.

**ACTION:** *Adopted by the House.*

## AMENDMENTS TO CONSTITUTION AND BYLAWS

Amendments to the Constitution and Bylaws may be introduced at any session of the House of Delegates. Amendments to the Bylaws may be acted upon 24 hours after introduction, while amendments to the Constitution must lie on the table until the next regular meeting of the House of Delegates.

Reference Committee No. 4 considers all pro-

posed amendments to both the Constitution and the Bylaws. Under the required waiting periods, all Constitutional amendments introduced in 1965 were brought before the House of Delegates for action in 1966. In some instances, proposed amendments to the Bylaws are also held over for one year, where they are entered as companions to proposed amendments to the Constitution.

## ACTIONS

Listed below are actions taken by the House of Delegates on all proposed amendments to the Constitution and Bylaws presented for action this year. A two-thirds affirmative vote is required for passage of all amendments. New language approved is shown in italics.

### CONSTITUTIONAL AMENDMENT

#### CONSTITUTIONAL AMENDMENT NO. 1-65

##### COMPOSITION OF COUNCIL

Introduced by: Council

**ACTION:** *Not adopted by the House.*

### BYLAW AMENDMENTS

#### BYLAW AMENDMENT NO. 1-66

##### RETIRED MEMBERSHIP

**Resolved:** That Chapter II, Section 4(a) of the Bylaws of the California Medical Association be amended by inserting the language in italics so that the section shall read:

“(a) Retired Members. The Council, on recommendation of any component society, may grant retired membership to those active and associate members who have ceased the practice of medicine to the extent and for reasons satisfactory to such component society and the Council, who have been active members of the Association for a total of 10 years prior thereto and who have paid dues for the current or immediately preceding year, *and those retired physicians who have moved to California and who have been active members of another state association or the American Medical Association for a total of 10 years prior thereto.*”

**ACTION:** *Adopted by the House.*

#### BYLAW AMENDMENT NO. 7-66

##### AFFILIATE MEMBERSHIP

**Resolved:** That Chapter II, Section 3, Paragraph (d) of the Bylaws of the California Medical Association be amended by adding the language in italics:

“(d) Qualifications for Affiliate Members. To be eligible for election to affiliate membership in a component society, an applicant must be, and must continue to be throughout the term of his membership, an intern, resident or house officer in an approved hospital within the county of the component society concerned. *A component society may grant affiliate membership to any phy-*

*sician not qualified for a class of membership referred to herein but whose qualifications are otherwise acceptable to the component society for affiliate membership.*”

**ACTION:** *Adopted by the House.*

#### BYLAW AMENDMENT NO. 8-66

##### PROVISIONAL MEMBERSHIP

**Resolved:** That Section 3, Chapter II, of the CMA Bylaws be amended by adding the words in italics and by deleting the words shown in parentheses, and to read:

“Section 3—Qualifications of Active, Associate, (and) Affiliate, *and Provisional Members*

“(a) Component Societies Sole Judges. Each component society shall, subject to the minimum requirements for eligibility as hereinbelow provided, determine the qualifications for membership for active, associate (or) , affiliate *or provisional* membership therein, and shall be the sole judge of the qualifications of applicant for such membership.”

and be it further

**Resolved:** That paragraph (e) be added under Chapter II, Section 3 of the Bylaws to read:

“(e) *Qualifications for Provisional Members. To be eligible for provisional membership in a component society, an applicant must possess all the qualifications necessary for active membership and be serving a provisional applicant term as may be required by the component society of all applicants for membership.*”

**ACTION:** *Adopted by the House.*

**Because a quorum was not present, the amendments listed below were not considered.**

#### BYLAW AMENDMENT NUMBERS

##### 22-65 Failure to Pay Dues

- 2-66 Termination, Suspension or Probation of Membership; Chapter II, Section 10(c)
- 3-66 Duties of District Councilors; Chapter VI, Section 8
- 4-66 Employment of Secretary, Assistant Secretaries, Editor and Associate Editors; Chapter VI, Section 12
- 5-66 Executive or Field Secretaries or Representatives; Chapter VI, Section 14
- 6-66 Duties of the Secretary, Executive Secretary and Field Representatives; Chapter IX, Section 2



- 9-66 Committee on Cardiovascular Diseases; Chapter IV, Section 2
- 10-66 Referendum Petitions; Chapter XII, Section 5
- 11-66 Addresses and Scientific Paper; Chapter IV, Section 6
- 12-66 Committee on Adverse Drug Reactions; Chapter IV, Section 2(i)
- 13-66 Committee on Veterans Affairs; Chapter

VII, Section (a)

- 14-66 Committee on Medical Aspects of Sports and Physical Fitness; Chapter VII, Section 1(c) (6)
- 15-66 The Election; Chapter XII, Section 6
- 16-66 Employment of Secretary, Assistant Secretaries, Editor and Associate Editor; Chapter VI, Section 12—Chapter XIX, Section 2—Chapter VI, Section 14

## FOR ACTION IN 1967

Six constitutional amendments were introduced in the 1966 House of Delegates and, under the terms of the Constitution, must lie on the table until the next regular meeting of the House of Delegates.

These proposed amendments are shown here for the information of the membership. In addition, the proposed Constitutional amendments are required to be printed in two issues of CALIFORNIA MEDICINE before it comes before the House of Delegates for action.

\* \* \*

### CONSTITUTIONAL AMENDMENT NO. 1-66

#### PHYSICIANS' BENEVOLENCE FUND

Introduced by: Council

**Resolved:** That Article IV, Section 6, of the Constitution of the CMA be amended by adding the language in italics and deleting the language shown in parentheses so it shall read:

"Section 6—Physicians' Benevolence Fund.

*"The Council shall determine from year to year, at the time of the Annual Meeting, (at least \$1.00 out of) the portion of the annual dues paid by each active member of the Association (shall) to be allocated to the Physicians' Benevolence Fund, Inc., a corporation, (and) funds so allocated shall be used for the purposes as set forth in that corporation's articles and bylaws."*

\* \* \*

### CONSTITUTIONAL AMENDMENT NO. 2-66

#### COMPOSITION OF THE COUNCIL

Introduced by: Council

**Resolved:** That Article III, Part B, Section 9, of the California Medical Association Constitution, be deleted and the following amendment be adopted:

*"The Council shall consist of:*

*"(a) Elected councilors from the councilor districts set forth in Section 10. Each councilor district shall be entitled to elect one (1) councilor for each 1,000 active members, or major fraction thereof, according to its membership as of the first day of September of the preceding year; provided, that each councilor district shall be entitled to a minimum of one (1) councilor.*

*"(b) Elected councilors from any one district shall not, at any time, exceed 40 per cent of the total Council membership.*

*"(c) The president, president-elect, immediate past president, speaker and vice-speaker.*

*"(d) The secretary and editor, when they are members of the Association, and one member of the Executive Committee of the Scientific Board, who shall be elected by the Executive Committee of that body from representatives of the scientific sections or members-at-large. These three persons shall be ex officio members of the Council without the right to vote."*

\* \* \*

### CONSTITUTIONAL AMENDMENT NO. 3-66

#### OFFICERS

Introduced by: Council

**Resolved:** That Article VI, Section 1, of the Constitution of the California Medical Association be amended by adding the language in italics and deleting the language shown in parentheses so that it shall read:

"Section 1.—Officers

*"The officers of this Association shall be a President, a President-Elect, (a Secretary) a Chairman of the Council, a Vice-Chairman of the Council, a Speaker of the House of Delegates, a Vice-Speaker of the House of Delegates and, when they are members of the Association, a Secretary and an Editor."*

## CONSTITUTIONAL AMENDMENT NO. 4-66

### CONSTITUTIONAL AMENDMENT TRANSFERRING AMADOR COUNTY TO FIFTH DISTRICT

Introduced by: Tenth District

WHEREAS, Article II, Part B, Section 10 of current CMA Bylaws places Amador County in Councilor District Number Ten; and

WHEREAS, only two of the 12 medical doctors licensed in Amador County maintain county society affiliation in a Tenth District society, the majority, because of travel patterns and hospital locations, preferring to affiliate with a county medical society in the Fifth District; and

WHEREAS, the Fifth and Tenth District delegations have endorsed such transfer of Amador County to the Fifth District; now, therefore, be it

**Resolved:** That Article II, Part B, Section 10 of the Constitution of the CMA be amended by adding the words in italics and deleting the words in parentheses, and to read:

"District Number Five, comprising *Amador*, Kern, Kings, Tulare, Fresno, Madera, Mariposa, Merced, Stanislaus, San Joaquin, Calaveras and Tuolumne Counties.

"District Number Ten, comprising Sacramento, (Amador,) Alpine, El Dorado, Placer, Nevada, Sierra, Yuba, Sutter, Yolo, Colusa, Glenn, Butte, Plumas, Tehama, Trinity, Shasta, Lassen, Modoc and Siskiyou Counties."

## CONSTITUTIONAL AMENDMENT NO. 5-66

### ESTABLISHING A SEPARATE COUNCILOR DISTRICT FOR THE COUNTY OF ORANGE

Introduced by: Orange County Medical Association

**Resolved:** That Article III, Part B, Section 10, Councilor District of the CMA Constitution be deleted and the following Section 10 substituted therefor.

"There are 12 districts as follows:

"District Number One, comprising San Diego.

"District Number Two, comprising Imperial, Riverside, San Bernardino, Mono and Inyo Counties.

"District Number Three, comprising Orange County.

"District Number Four, comprising the County of Los Angeles.

"District Number Five, comprising Ventura, Santa Barbara and San Luis Obispo Counties.

"District Number Six, comprising Kern, Kings, Tulare, Fresno, Madera, Mariposa, Merced, Stanislaus, San Joaquin, Calaveras and Tuolumne Counties.

"District Number Seven, comprising Monterey,

San Benito, Santa Cruz, Santa Clara and San Mateo Counties.

"District Number Eight, comprising San Francisco County.

"District Number Nine, comprising Alameda County and Contra Costa County.

"District Number Ten, comprising Marin, Solano, Napa, Sonoma, Lake, Mendocino, Humboldt and Del Norte Counties.

"District Number Eleven, comprising Sacramento, Amador, Alpine, El Dorado, Placer, Nevada, Sierra, Yuba, Sutter, Yolo, Colusa, Glenn, Butte, Plumas, Tehama, Trinity, Shasta, Lassen, Modoc and Siskiyou Counties.

"District Number Twelve, consisting of any society which is not limited as to geographical area, or the area of which overlaps the area covered by one or more existing component societies; such society and its members shall not be considered to be members of any other councilor district."

## CONSTITUTIONAL AMENDMENT NO. 6-66

### REVISION OF DISTRICT ONE

Representing: Imperial

Introduced by: Burke E. Schoensee

**Resolved:** That Article III, Part B, Section 10 of the Constitution be amended by revising District Number One to include San Diego and Imperial Counties, and that Imperial County be deleted from District Number Two, and that otherwise said Section remain unaltered.

## AMENDMENT CALIFORNIA MEDICAL ASSOCIATION BYLAWS

Resolution No. 97-66

Committee 4

Introduced by: Los Angeles Delegation

WHEREAS, the Constitution of the California Medical Association was amended in 1962, to provide that the California Medical Association could issue a charter to a component county medical society, *or any established component district, of at least 300 members of a county society, which has exercised option to withdraw from that county society and set up a separate component society*, subject to a two-thirds affirmative vote of the Delegates of the House of Delegates of the California Medical Association, approving such withdrawal and the issuance of a charter; and

WHEREAS, the Bylaws of the California Medical Association were not amended in 1962, to provide a procedure for an orderly exercise, by an established component district of a county medical society, of the option to withdraw from the County Medical Society and to become autonomous; and

WHEREAS, a procedure should be established by



the House of Delegates of the California Medical Association; now, therefore, be it

**Resolved:** That the Speaker of the House of Delegates be hereby authorized to appoint an Ad Hoc committee of this House of Delegates to study and investigate the problem of the establishment of an orderly procedure for an established component district of a county medical society to exercise

option to withdraw from the county medical society and become autonomous and said ad hoc committee to submit a proposed bylaw amendment to the California Medical Association Bylaws that would detail and provide such an orderly procedure.

**ACTION:** *Because a quorum was not present, this resolution was not considered.*

## REFERENCE COMMITTEE RECOMMENDATIONS

*Reference Committees are encouraged to comment on any activity of the California Medical Association that comes to their attention. If these observations or recommendations are not directed toward a specific resolution, constitution or bylaw amendment, they are recorded in this section.*

### REFERENCE COMMITTEE NO. 1

It is recommended that:

(1) The California Medical Education and Research Foundation report its activities to the House of Delegates in the *Annual Reports Bulletin*;

(2) The Bureau on Research and Planning publish an index of the data it has available so that any physician who wishes may request specific information the Bureau has on deposit. Copies of studies need not be voluntarily distributed.

The committee observed that the growth of the Bureau of Research and Planning has been rapid and recognized that there is an optimum to the size of such an activity and a limit to the financial support that can be given it.

### REFERENCE COMMITTEE NO. 2

1. That the House of Delegates express to the family of the late Mr. Hunton, its gratitude for his many contributions.

*Recommend that this be done by a letter from Doctors Quinn and MacLaggan.*

2. That all members of the Association should be more adequately informed on how cost estimates are projected and the various steps and stages through which the budget is processed before reaching the House of Delegates for consideration.

*Recommend that the Finance Committee prepare an article for California Medicine.*

3. That the CMA staff prepare a cost estimate on each resolution introduced to the House of Delegates, such cost estimate to be given to the

appropriate Reference Committee at the time of its hearing and again when presented to the House of Delegates. Also recommended that a similar procedure be followed by the Council when considering initiation of unbudgeted activities.

*Recommend that this be referred to the Finance Committee and the staff.*

4. That the Council evaluate the proper role of this Association in the financial support of medical libraries and recommend a policy to be considered by the House of Delegates at its next annual meeting.

*Recommend that this be referred to an ad hoc committee composed of the chairmen of the Scientific Board, Committee on Continuing Medical Education, Finance Committee, a member of the House of Delegates Reference Committee No. 2 and the presidents of those county medical societies having libraries.*

5. That the Council be instructed to place an appropriate amount of income into the reserves each year until this objective (adequate reserve) has been accomplished.

*Recommend that this be referred to the Finance Committee.*

6. That the Council disseminate appropriate information to the entire membership regarding the need for the increases in dues through established publications.

*Recommend referral to the Finance Committee and the Commission on Communications.*

### REFERENCE COMMITTEES NOS. 3, 3A and 3B

Recommendations are a part of the report on the resolutions.

### REFERENCE COMMITTEE NO. 4

Recommendations are a part of the report on the constitutional amendment or bylaw change.

### REFERENCE COMMITTEE ON THE CALIFORNIA PHYSICIANS' SERVICE

Recommendations are a part of the report on the resolutions.

## Council Meeting Minutes

*Tentative Draft: Minutes of the 519th Meeting of the Council, Los Angeles, Biltmore Hotel, 18-23 March 1966.*

The meeting was called to order by Chairman Anderson in the Biltmore Hotel, Los Angeles, on Friday, 18 March 1966, at 4:00 p.m. and thereafter was recessed and reconvened on each of the succeeding days through 23 March 1966.

### *Roll Call*

Present were President Teall, President-elect MacLaggan, Speaker Quinn, Vice-Speaker Telford, Editor Dwight L. Wilbur, Secretary Hosmer and Councilors Isenhour, Melone, Todd, Gooel, Taw, Bullock, O'Connor, Ham, Rogers, Maguire, Burnett, Richard S. Wilbur, Miller, Watts, Fenlon, Kay, Kaiser, Anderson, Yant, Grunigen, Shaw and Immediate Past President Doyle.

A quorum present and acting.

Present by invitation were Messrs. Clancy, Collins, Thomas, Eberlein, Whelan, Bowman, Blackley, Clark, Mrs. Griffith, Doctor Miller, Mrs. Redfern and Miss Price of CMA staff; Messrs. Hassard and Huber, legal counsel; component society executives Scheuber of Alameda-Contra Costa, Rideout of Butte-Glenn, Geisert of Kern, Lingerfelt of Fresno, Dalbec of Los Angeles, Colvin of Monterey, Sommerville of Napa, Bannister of Orange, Walters of Riverside, Dochterman of Sacramento, Donmyer of San Bernardino, Neick of San Francisco, Thompson of San Joaquin, Wood of San Mateo, Marvin of Santa Barbara, Donovan of Santa Clara, Brown of Sonoma, Whitehall of Stanislaus, Bruce of Tulare, Jackson of San Diego; Doctor William Thompson and Messrs. Saylor, Nyren, Potloff, Babb, and Heller of California Physicians' Service; Messrs. Read, Salisbury and Brown of the Public Health League; Mr. Jerry Gould of the AMA; Mr. Richard Layton of AMPAC; Dr. Ben H. Dean, president of the California Veterinary Medical Association; Doctor James V. Lowry, director of the Department of Mental Hygiene, and others.

### 1. *Minutes for Approval*

On motion duly made and seconded, minutes of the 518th meeting of the Council, held 19 February 1966, were approved as distributed.

### 2. *Membership*

(a) On motion duly made and seconded, two members whose dues were delinquent and now paid, were reinstated.

(b) On motion duly made and seconded, seven applicants were voted election to Associate Membership. These were: Wm. Clark Cooper, William Mandel, Alameda-Contra Costa County; Reginald Rood, Napa County; Donald Lee Donohugh, Orange County; Roswell L. Hull, San Benito County; Lourdes O. Agcaoili and Frank G. Moody, San Francisco County.

(c) On motion duly made and seconded, 13 members were voted election to Retired Membership. These were: Elenore J. Erickson, Maude Lee Etheredge, Alameda-Contra Costa County; William G. Patton, Saul S. Robinson, Los Angeles County; Horace A. Hall, San Bernardino County; Harry Bramwell, Thornton Craig Russell, San Joaquin County; Warren R. Austin, Eustace Lincoln Benjamin, Santa Barbara County; Marion C. Collins, Stanislaus County; Robert A. Blossom, Walter P. Streitell, Ventura County; Phillip B. Hoffman, Yuba-Sutter-Colusa County.

(d) On motion duly made and seconded, a reduction of dues was voted for 24 members for reasons of prolonged illness or postgraduate education.

### 3. *Resignation of Councilor Wilson*

Chairman Anderson presented a letter from Doctor Llewellyn E. Wilson announcing his resignation as a CMA Council from the Second District, effective immediately prior to the opening of the House of Delegates meeting. Representatives of the Second District nominated Doctor Henry V. Eastman of Tustin to fill Doctor Wilson's unexpired term.

**ACTION:** Voted to name Doctor Henry V. Eastman of Tustin to fill the unexpired Second District Councilor term of Doctor Llewellyn E. Wilson.

### 4. *Recognition of Doctor Roberta Fenlon*

For several months Councilor Fenlon has served as a special consultant to the Bureau of Health Insurance (Social Security Administration) assisting its staff in the development of regulations and procedures under Public Law 89-97. Chair-



man Anderson read correspondence from the Board of Trustees of the American Medical Association commending Doctor Fenlon on her contribution to American medicine in this regard. The CMA Council joined in this commendation.

#### 5. *Resolutions for the 1966 House of Delegates*

Two proposed resolutions (which were submitted to the CMA subsequent to the seven-day deadline) were presented to the Council for possible introduction into this session of the House of Delegates.

(a) Resolution proposing study of the CAL-MED plan by an ad hoc committee of the House of Delegates (submitted by several delegates from Los Angeles County).

**ACTION:** *Voted to submit the CAL-MED resolution to the House of Delegates. (Resolution 106-66.)*

(b) Resolution urging the Governor to appoint a physician to the State Veterans Board (submitted by Doctor Charles Hudson of Oakland). The Council did not believe the resolution was of emergency nature but could be handled without bringing the subject matter before the House.

**ACTION:** *Voted to deny submission of this as an emergency resolution.*

#### 6. *California Volunteers for Political Action (CALPAC)*

A statement supporting the concepts of political education and political action as promoted by the California Volunteers for Political Action (CALPAC) was presented to the Council.

**ACTION:** *Voted to include the intent of the statement in the supplemental report of the Council to be presented to the House of Delegates.*

#### 7. *Committee on Committees*

President-Elect MacLaggan presented the list of nominees for appointments to CMA commissions and committees for the 1966-67 year. Several amendments and changes in the list, as previously distributed, were recommended by the Committee on Committees. These were:

(a) Recommended that Doctor Richard Lescoc of Torrance be substituted for Doctor Stanley Skillicorn on the Committee on Medicine and Religion.

**ACTION:** *Voted approval of the change.*

(b) Recommended that Doctor J. Blair Pace

of Oceanside be added to the Committee on Continuing Medical Education.

**ACTION:** *Voted approval of the recommendation.*

(c) Recommended the addition of Doctor Don Harper Mills of Los Angeles as a consultant to the Medical Review and Advisory Committee.

**ACTION:** *Voted approval of the recommendation.*

(d) Recommended that the name of the Bureau of Research & Planning (which was to be changed to the Bureau of Research by action of the Council at its February 1966 meeting) remain as it is until current contractual commitments of the Bureau are fulfilled.

**ACTION:** *Voted to retain the name of the "Bureau of Research and Planning" until its existing contractual commitments are terminated.*

(e) Recommended the following Council nominations for terms on the Board of Trustees of California Physicians' Service: Nomination of Doctor Gregory C. Murray of Los Angeles and Mr. Ransom Cook of San Francisco to succeed themselves; Nomination of Doctors Carl E. Anderson of Santa Rosa, Ralph C. Burnett of Bakersfield, M. M. Haskell of Long Beach and Carl Goetsch of Oakland to fill other terms expiring.

**ACTION:** *Voted approval of these six Council nominees to the Board of Trustees of California Physicians' Service.*

The entire list of Council recommendations for commission and committee appointments, as amended, was then presented for formal submission to the House of Delegates.

**ACTION:** *Voted to submit the amended list of commission and committee appointments for 1966-67 to the House of Delegates.*

#### 8. *Report of the President*

President Teall reported on several matters pertaining to the Association in which he had been involved since the previous meeting of the Council. These included a progress report on the "grant application" submitted by the California Coordinating Committee on Heart Disease, Cancer and Stroke to the Department of Health, Education and Welfare (under Public Law 89-239); discussions with state governmental representatives regarding fees and other problems of implementation of Assembly Bill 5; a special luncheon meeting in San Francisco with Doctor Philip R. Lee, assistant secretary of Health, Education and Welfare; and results of the 9 March meeting of the CMA Task Force on Public Law 89-97.

## 9. *Committee for Emergency Action*

Doctor Anderson reviewed previous actions of the CMA with regard to supporting certain budgetary allocations of the State Department of Public Health, some of these allocations being strongly challenged by the legislative analyst in the last budget session of the Legislature and again in this session. The legislative analyst this year was recommending again the deletion of the budget for the Bureau of Occupational Health of the Department of Public Health. Inasmuch as the CMA previously had supported strongly the retention of the Bureau of Occupational Health, the Committee for Emergency Action made an effort to support this position in this session of the Legislature.

**ACTION:** *Voted to affirm the decision and action of the Committee for Emergency Action.*

## 10. *Ad Hoc Committee on Resolution No. 19-65* (Establishment of a new Commission on Medical Economics)

Several months ago an ad hoc committee of the Council was designated to meet with the author of House of Delegates Resolution No. 19-65 to determine in more depth the concepts underlying his recommendation to have the CMA establish a new Commission on Medical Economics. After meeting with the author of the resolution, the ad hoc committee (Doctor Milo A. Youel, chairman) recommended "that the Council urge the Commission on Medical Services and the Bureau of Research & Planning along with CPS to continue their vigorous studies in the broad field of medical economics and the continued awareness of the need for imaginative approaches."

**ACTION:** *Voted to "receive" the report of the ad hoc committee and refer it to the Committee on Organizational Review and Planning.*

## 11. *Medical Executives Conference*

Mrs. Olive Neick reported that the members of the conference (on Friday 18 March) had elected Mr. Rueben Dalbec, executive director of the Los Angeles County Medical Association, as chairman of the Medical Executives Conference for the 1966-67 year. She also reported that the medical executives voted to recommend to the Council that three executive secretaries be asked to serve in an advisory committee to the group planning the 1967 Conference on Component Society Officers; these three executives to be the MEC chairman, the executive secretary serving the society from which

the physician chairman of the planning committee comes, and one member-consultant at large.

**ACTION:** *Voted to accept the recommendation of the Medical Executives Conference that three of its members act in an advisory capacity to the physician group planning the 1967 Conference of Component Society Officers.*

## 12. *Commission on Community Health Services*

Doctor Kay presented a request from the State Department of Education that the CMA act as a co-sponsor of a California Physical Fitness Clinic at the College of San Mateo in May.

**ACTION:** *Voted approval for CMA "co-sponsorship" of this program.*

Recent actions of the American Medical Association and the California Hospital Association pertaining to the posting of "hospital signs" on major highways and thoroughfares were reviewed by Doctor Kay. He presented a request from the California Hospital Association that CMA, through its Committee on Traffic Safety, support CHA efforts to assure that adequate "hospital designation signs" be installed on freeways and other major roads throughout California.

**ACTION:** *Voted to support California Hospital Association efforts to secure "adequate hospital designation signs" on California roads.*

Doctor Leo Snyder, chairman of the Committee on Rural Health, described a proposed program which would involve medical students working as externs in rural areas of the state during the summer months.

**ACTION:** *Voted to accept the report of the Committee on Rural Health.*

## 13. *Commission on Public Agencies*

Doctor Miller presented a report from the Committee on Occupational Health and Rehabilitation pertaining to Resolution No. 26-65 (Definitions of Disability).

**ACTION:** *Voted to accept the report, containing the Definitions of Disability, as submitted by the Committee.*

The Committee on Public Health reported that funds for travel for the six regional rabies advisory committees were deleted from the State Department of Public Health's 1965-66 budget by the Senate Finance Committee.

**ACTION:** *Voted to express support of the Department of Public Health in its efforts for restoration of rabies advisory board travel expenses and reestablishment of full time support for the two position*



*class public health veterinarians in the Department's 1966-67 budget.*

The Committee on Public Health asked the Council to reconsider its previous position (17 January 1965) pertaining to the Congestive Heart Failure Follow-up Program of the State Department of Public Health. Previously, the Council said the specific research project should be conducted under the auspices of a school of medicine.

**ACTION:** *Voted to amend the Council action of 17 January 1965 pertaining to Congestive Heart Failure Programs by adding at the end the words, "or a component medical society."*

(The full action, as amended, now reads: "Voted to inform the coordinating agency that while such studies may be of value, it was felt that they should be undertaken as a specific research project under the auspices of a school of medicine or a component medical society.")

**ACTION:** *Voted to accept the full report, as amended, of the Committee on Public Health.*

#### 14. Scientific Board

The Scientific Board through its chairman, Doctor Edward B. Shaw, received a request from The National Foundation-March of Dimes that the CMA co-sponsor a symposium on "New Directions in Human Genetics" in February 1967.

**ACTION:** *Voted to disapprove the request for CMA co-sponsorship.*

Doctor Shaw, who is retiring from the chairmanship of the Scientific Board after a three-year term, made a detailed report on activities of the past three years and some recommendations for the future. One of his recommendations was that the Chairman of the Scientific Board be given a vote on the CMA Council.

**ACTION:** *Voted to support the amendment before the House of Delegates which would give the Chairman of the Scientific Board a vote on the Council.*

**ACTION:** *Voted to extend thanks to Doctor Shaw for his distinguished leadership of the Scientific Board during the past three years.*

#### 15. Appointment to the State Veterans Board

Doctor Charles Hudson of Oakland urged the Council to ask Governor Brown to appoint a physician to the State Veterans Board. The physicians recommended were Dr. Robert Leake of Sacramento and E. J. Twigg of Oakland.

**ACTION:** *Voted to recommend to the Governor of California that Dr. Robert Leake of Sacramento and*

*Edvard Twigg of Oakland be appointed to the State Veterans Board.*

#### 16. Commission on Hospital Affairs

In response to Resolution No. 41-65, the Committee on Health Facilities Planning attempted to determine the extent of financial support given by component medical societies to voluntary regional planning efforts. As a result of this study the Committee recommended that (1) CMA presently provide only moral, not financial support to regional planning groups, and (2) the specific request for funds from the North Coast Health Facilities Planning Association should not be honored until the interest and active participation in the support of that association by the local component medical society is more definitely established.

**ACTION:** *Voted to accept both recommendations of the Committee on Health Facilities Planning.*

#### 17. Bylaw Amendments Before the 1966 House of Delegates

Due to ambiguity in the wording of three proposed bylaw amendments already mailed to the House (4-66, 5-66 and 6-66), it was recommended that a substitute bylaw amendment be prepared and presented to the House in place of the three listed above.

**ACTION:** *Voted to substitute a clarifying bylaw amendment (numbered 17-66) for presentation to the 1966 House of Delegates.*

#### 18. Council Resolution on "Medicare Education"

A resolution concerning a national educational program on Medicare was presented to the Council. The resolution stated:

WHEREAS, there is already great confusion as to the details of Medicare, the program of hospital and medical care, paid for by wage earners and self-employed, for the benefit of those over 65; and

WHEREAS, unless the so-called benefits, as well as the exemptions, the deductibles, the part-payment for medical services and other rules and regulations are fully explained to this over-age group all complaints and dissatisfactions are more than likely to be attributed to physicians and hospitals; and

WHEREAS, it is equally true that over-use and abuses by either physicians, hospitals or patients is likely to jeopardize Medicare's total objective; and

WHEREAS, it is to the interest of the public, the profession and the hospitals that as much confusion as possible be erased and replaced with understanding; now, therefore, be it

*Resolved:* That the California Medical Association insist that the American Medical Association institute a nationwide television program of fundamental Medicare education; and be it further

*Resolved:* That the California Medical Association invite the American Hospital Association to participate in the preparation and payment of said educational program; and be it further

*Resolved:* That the California Medical Association, in conjunction with the California Hospital Association, prepare pilot material for presentation before the House of Delegates of the American Medical Association at the June meeting in Chicago, 1966.

*ACTION: Voted to approve the Council resolution.*

19. *Ad Hoc Committee to Study Quality of Radiologic Films*

Through correspondence to the Council, Doctor L. Henry Garland requested reconsideration of the report of the ad hoc Committee to Study Quality of Radiologic Films which was accepted by the Council on 11 December 1965. No action was taken on the request of Doctor Garland.

20. *Meeting Dates of the Council*

The Council approved a list of tentative Council meeting dates for the 1966-67 year.

21. *Utilization of Income for Former County/Charity Patients*

Discussion was heard on the potential problems involved in utilization of income for care of former clinic or charity patients who are drawn into "mainstream" care by Public Law 89-97 (but who are still cared for in county hospitals, medical school clinics and public institutions).

*ACTION: Voted to ask the Task Force on Public Law 89-97 to study this problem and report to the Council in May. (Resolution No. 56-66, passed by the House of Delegates, refers to this problem and will be considered by the Task Force.)*

*Adjournment*

There being no further business to come before it, the meeting was adjourned on Wednesday, 23 March 1966, at 8:50 a.m.

CARL E. ANDERSON, M.D., *Chairman*  
MATTHEW N. HOSMER, M.D., *Secretary*

*Tentative Draft: Minutes of the 520th Meeting of the Council, Los Angeles, Biltmore Hotel, 23 March 1966.*

The meeting was called to order by President\* MacLaggan in the Biltmore Hotel, Los Angeles, on Wednesday, 23 March 1966, at 4:00 p.m.

*Roll Call*

Present were President MacLaggan, President-Elect Morrison, Speaker Quinn, Vice Speaker Telford, Editor Dwight L. Wilbur, Secretary Weyrauch and Councilors Isenhour, Melone, Todd, Goebel, Taw, O'Connor, Rogers, Burnett, Richard S. Wilbur, Miller, Watts, Fenlon, Kay, Kaiser, Anderson, Yant, Boyle, Crum, Eastman and Immediate Past President Teall.

A quorum present and acting.

Present by invitation were Messrs. Thomas, Collins and Clark of CMA staff; Mr. Hassard, legal counsel; and others.

1. *Election of Officers*

On nominations duly made and seconded, the following were unanimously elected to the positions shown: Chairman, Carl E. Anderson; Vice-Chairman, Albert G. Miller.

2. *Administrative Appointments*

Doctor Matthew N. Hosmer had previously requested the Council not to consider him for reappointment to the office of secretary and the Council had previously expressed to Doctor Hosmer deep appreciation for his devoted service over the years.

On nominations duly made and seconded, the following were unanimously appointed to the positions shown: Secretary, Helen B. Weyrauch; Editor, Dwight L. Wilbur; Executive Director, Mr. Howard Hassard; Legal Counsel, Peart, Barty & Hassard.

3. *Committee Appointments*

Chairman Anderson, on nominations presented by the Committee on Committees and the Council concurring, made the following committee appointments:

*Bureau of Research and Planning*—Samuel Sherman, chairman, San Francisco; James Powell, Stockton; John Sheehy, Riverside; H. Russell Fisher, Glendale; and Harold Wilkins, Los Angeles. Ex-officio, Malcolm S. M. Watts and Ralph C. Teall. Consultant: Gerald W. Shaw.

*Committee on Role of Medicine in Society*—Malcolm



S. M. Watts, chairman, San Francisco; Malcolm C. Todd, Long Beach; Elmer Goel, Beverly Hills; Gerald Besson, Sunnyvale; Sanford Feldman, San Francisco; Burt L. Davis, Palo Alto. Ex-officio, Samuel R. Sherman and Ralph C. Teall.

*Committee on Organizational Review and Planning*—Ralph C. Teall, chairman, Sacramento; John Saidy, San Mateo; and Jean Crum, Los Angeles. Ex-officio, Samuel R. Sherman and Malcolm S. M. Watts.

*CPS Advisory Study Committee*—Donald D. Lum, chairman, Alameda; Carl E. Anderson, Santa Rosa; Gerson Biskind, San Francisco; Clyde L. Boice, Palo Alto; Bert L. Halter, San Francisco; Donald P. Hause, Sacramento; Paul I. Hoagland, Pasadena; Joseph Telford, San Diego; Henry K. Oetting, Los Angeles; and Edward J. Twigg, Oakland.

*Liaison Committee to CPS*—James C. MacLaggan, San Diego; John G. Morrison, San Leandro; William F. Quinn, Los Angeles; and Carl E. Anderson, Santa Rosa. (This is the Committee for Emergency Action.)

*Committee on Legislation*—Dan O. Kilroy, chairman, Sacramento; Stuart C. Knox, Los Angeles; Harold E. Wilkins, Downey; John Rumsey, San Diego; and Samuel R. Sherman, San Francisco.

*Advisory Board to Woman's Auxiliary*—James C. MacLaggan, San Diego; John G. Morrison, San Leandro; William F. Quinn, Los Angeles; Carl E. Anderson, Santa Rosa; and Eugene Hoffman, Los Angeles.

*Ad hoc Committee on Workmen's Compensation*—Carl E. Anderson, chairman, Santa Rosa; Francis J. Cox, San Francisco; Dan O. Kilroy, Sacramento; Packard Thurber, Jr., Los Angeles; and Francis E. West, San Diego. Consultant: Mr. Ben H. Read.

*Benevolence Fund Operating Committee*—Clyde L. Boice, chairman, Palo Alto; Alexander Fraser and Don C. Musser, San Francisco; Elizabeth Mason Hohl and Dudley M. Cobb, Jr., Los Angeles; and George Wolf, Fresno.

*Task Force on Public Law 89-97*—Ralph C. Teall, chairman, Sacramento; James C. MacLaggan, San Diego; Bert L. Halter, San Francisco; Roger Isenhour, San Diego; Albert G. Miller, San Mateo; Malcolm C. Todd, Long Beach; Milo A. Youel, San Diego; Dan O. Kilroy, Sacramento; Samuel R. Sherman, San Francisco; John A. Bullis, Los Angeles; Richard S. Wilbur, Palo Alto; Joseph F. Boyle, Los Angeles; Henry V. Eastman, Tustin; H. Dean Hoskins, Oakland; Donald C. Harrington, Stockton; A. B. Sirbu, San Francisco; and John G. Morrison, San Leandro.

*Task Force on Public Law 89-239*—James C. MacLaggan, chairman, San Diego; Ralph W. Burnett, Bakersfield; Roger Egeberg, Los Angeles; Sanford E. Feldman, San Francisco; Carl Goetsch, Berkeley; George Griffith, Los Angeles; W. Kenneth Jennings, Santa Barbara; James Martin, Sacramento; John T. Saidy, San Mateo; Justin J. Stein, Los Angeles; Richard Taw, Los Angeles; Francis E. West, San Diego; Robert Westphal, Modesto; Omer Wheeler, Riverside; Malcolm S. M. Watts, San Francisco; Ralph C. Teall, Sacramento; and Samuel R. Sherman, San Francisco.

*Finance Committee*—Harold Kay, chairman, Oakland; Roger C. Isenhour, San Diego; Frank C. Melone, Ontario; Joseph W. Telford, San Diego; and Malcolm C. Todd, Long Beach.

*Committee on Committees*—John G. Morrison, chairman, San Leandro; Ralph W. Burnett, Bakersfield; William F. Kaiser, Berkeley; Joseph P. O'Connor, Pasadena;

Malcolm S. M. Watts, San Francisco; Henry Eastman, Tustin; Richard S. Wilbur, Palo Alto; James H. Yant, Sacramento; Wilbur G. Rogers, Glendale; James C. MacLaggan, San Diego; William F. Quinn, Los Angeles; Carl E. Anderson, Santa Rosa; and Ralph C. Teall, Sacramento.

*CMA Representatives on the Joint Council to Improve Health Care of the Aged*—Thomas Elmendorf, Willows, term expiring 1969.

*Program Committee for the 1967 Annual Conference of Component Society Officers*—Dale W. Ritter, chairman, Chico; J. Brandon Bassett, Oakland; Robert Mills, San Rafael; Sam Peck, San Diego; Max Millar, Fresno; and Henry Eastman, Tustin. Consultants: L. Morgan Boyers, Rueben Dalbec and Eugene Rideout.

*CMA-CHA Advisory Board*—Bert L. Halter, San Francisco; John T. Saidy, San Mateo; Joseph W. Telford, San Diego; Glenn A. Pope, Sacramento; and John Lungren, Long Beach. Ex-officio, James C. MacLaggan, John G. Morrison, William F. Quinn, Carl E. Anderson.

*CMA Councilors on CPS Board of Trustees*—Roberta Fenlon, San Francisco; Wilbur G. Rogers, Glendale; and Richard S. Wilbur, Palo Alto.

#### 4. Editorial Board of "California Medicine"

Editor Dwight L. Wilbur presented a list of recommendations for reappointment and initial appointment to the Editorial Board of CALIFORNIA MEDICINE.

Reappointment: Orthopedics, Don King, San Francisco; Otolaryngology, Charles P. Lebo, San Francisco; Plastic Surgery, George V. Webster, Pasadena, and Biostatistics (consultant), Dr. Jacob Yerushalmy, Berkeley.

Initial Appointment: Internal Medicine, Donald W. Petit, Los Angeles; General Surgery, Richard E. Gardner, San Francisco; General Practice, Robert L. Hippen, San Diego; Radiology, Robert B. Engle, Pasadena; Pharmacology, Sydney M. Finegold, Los Angeles and Obstetrics and Gynecology; Ernest W. Page of San Francisco and William J. Dignam of Los Angeles.

**ACTION:** Voted to accept the list of recommendations for the Editorial Board of "California Medicine."

#### 5. Procedures of the House of Delegates

Several suggestions were received from various delegates, alternates and councilors as to revisions in the procedures and timing of meetings of the House of Delegates.

**ACTION:** Voted to ask the Speaker of the House of Delegates to evaluate the procedures and timing of the meetings.

#### 6. Pilot Film for "Medicare" Education

At its 519th meeting the Council approved a resolution calling for development of medicare

information films in California and nationally, with the cooperation of AMA and the American Hospital Association. Doctor Homer Pheasant suggested the development of a pilot film to initiate the project.

**ACTION:** *Voted to ask the CMA Communications Department to explore the proposal of Doctor Pheasant and report to the Committee for Emergency Action.*

#### 7. Resolution No. 106-66 (Cal-Med)

The Council asked for immediate referral of the 1966 resolution dealing with the CAL-MED plan proposed by California Assembly Speaker Jesse Unruh.

**ACTION:** *Voted to refer House of Delegates Resolution No. 106-66 (CAL-MED) to the CMA Task Force on Public Law 89-97.*

#### 8. Recruitment and Training of Paramedical Personnel

Doctor Dwight L. Wilbur and others proposed that CMA initiate immediately a study program on the problems of recruitment, training and supervision of paramedical personnel—especially in light of congressional interest at the national level.

**ACTION:** *Voted to refer this subject to the Committee on Organizational Review and Planning.*

#### 9. Time and Place of Next Meeting

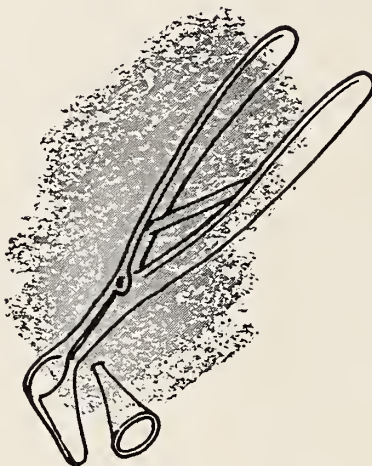
The chairman announced that the next regular meeting of the Council would be held in San Francisco (Hilton Inn) on Saturday, 7 May 1966.

#### Adjournment

There being no further business to come before it, the meeting was adjourned at 4:29 p.m.

CARL E. ANDERSON, M.D., *Chairman*

HELEN B. WEYRAUCH, M.D., *Secretary*





## In Memoriam

ALEXANDER, CHARLES BURTON, Palm Desert. Died 10 April 1966, in Palm Springs, aged 71. Graduate of Loyola University School of Medicine, Chicago, Illinois, 1917. Licensed in California in 1923. Doctor Alexander was a member of the Riverside County Medical Association.



CRAIG, LYLE GLENN, Pasadena. Died 6 April 1966, in Pasadena, aged 69, of metastatic carcinoma. Graduate of Rush Medical College, Chicago, Illinois, 1924. Licensed in California in 1924. Doctor Craig was a member of the Los Angeles County Medical Association.



EMERSON, CHARLES VAN ARSDALE, Montebello. Died 9 March 1966, in Montebello, aged 63, of myocardial infarction. Graduate of the University of Southern California School of Medicine, Los Angeles, 1933. Licensed in California in 1933. Doctor Emerson was a member of the Los Angeles County Medical Association.



HENDERSON, H. EDWIN, Santa Barbara. Died 13 April 1966, in Santa Barbara, aged 73. Graduate of the University of Kansas School of Medicine, Lawrence-Kansas City, 1918. Licensed in California in 1919. Doctor Henderson was a member of the Santa Barbara County Medical Society.



JOHNSON, EDITH E., Palo Alto. Died 7 March 1966, in Menlo Park, aged 93. Graduate of Cornell University Medical College, New York, 1907. Licensed in California in 1907. Doctor Johnson was a retired member of the Santa Clara County Medical Society and the California Medical Association, and an associate member of the American Medical Association.



KAWALEK, MARCEL I., Anaheim. Died 12 March 1966, in Anaheim, aged 53, of coronary artery disease. Graduate of Medizinische Fakultät der Universität, Wien, Germany, 1938. Licensed in California in 1952. Doctor Kawalek was an associate member of the Orange County Medical Association.



KNOWLTON, JOHN C., Kern City. Died 26 August 1965, in Oildale, aged 75, of bronchopneumonia. Graduate of the College of Osteopathic Physicians and Surgeons, Los Angeles, 1924. Licensed in California in 1924. M.D. degree from California College of Medicine, 1962. Doctor Knowlton was a member of the Forty First Medical Society.



KOENNECKE, CLARENCE HERBERT, Los Angeles. Died 17 April 1966, in Los Angeles, aged 62, of cardiac arrest, coronary arteriosclerotic disease. Graduate of Northwestern University Medical School, Chicago, Illinois, 1934. Licensed in California in 1943. Doctor Koennecke was a member of the Los Angeles County Medical Association.



ORWOLL, HAROLD SIEFEST, Sunnyvale. Died 26 February 1966, in Sunnyvale, aged 51. Graduate of The University of Chicago, The School of Medicine, Illinois, 1946. Licensed in California in 1953. Doctor Orwoll was a member of the Santa Clara County Medical Society.

PRICE, EDGAR, Los Angeles. Died 29 March 1966, in Beverly Hills, aged 64, of cerebral thrombosis. Graduate of Medizinische Fakultät der Universität, Wien, Austria, 1928. Licensed in California in 1942. Doctor Price was a member of the Los Angeles County Medical Association.



ROBERTS, B. D., Anaheim. Died 3 April 1966, in Anaheim, aged 62, of coronary artery disease. Graduate of the University of Illinois College of Medicine, Chicago, 1935. Licensed in California in 1945. Doctor Roberts was a member of the Orange County Medical Association.



RYAN, CLARK DAVID, Laguna Beach. Died 29 April 1966, in Laguna Beach, aged 75. Graduate of the College of Physicians and Surgeons, Medical Department, University of Southern California, Los Angeles, 1918. Licensed in California in 1918. Doctor Ryan was an associate member of the Los Angeles County Medical Association.



SMITH, GERALD WALKER, Burlingame. Died 10 April 1966, aged 64, of heart disease. Graduate of the University of Kansas School of Medicine, Lawrence-Kansas City, 1926. Licensed in California in 1954. Doctor Smith was a member of the San Mateo County Medical Society.



SPROUL, WILLIAM MATTHEW, San Jose. Died 5 April 1966, in San Jose, aged 66. Graduate of State University of Iowa College of Medicine, Iowa City, 1926. Licensed in California in 1958. Doctor Sproul was an associate member of the Santa Clara County Medical Society.



STADLER, ERMAN, San Jose. Died 11 March 1966, in San Jose, aged 67. Graduate of St. Louis University School of Medicine, Missouri, 1921. Licensed in California in 1936. Doctor Stadler was a member of the Santa Clara County Medical Society.



STROUSE, SOLOMON, Beverly Hills. Died 28 April 1966, in Beverly Hills, aged 83, of arteriosclerotic heart disease. Graduate of Johns Hopkins University School of Medicine, Baltimore, Maryland, 1906. Licensed in California in 1936. Doctor Strouse was a retired member of the Los Angeles County Medical Association and the California Medical Association, and an associate member of the American Medical Association.



TATKIN, SYLVAN OSCAR, Tujunga. Died 11 April 1966 in Sunland, aged 50, of coronary artery disease. Graduate of the University of Minnesota Medical School, Minneapolis, 1947. Licensed in California in 1949. Doctor Tatkin was a member of the Los Angeles County Medical Association.



VERBRYCK, GEORGE GARRISON, Long Beach. Died 11 April 1966, in Lynwood, aged 70, of a brain tumor. Graduate of Rush Medical College, Chicago, Illinois, 1919. Licensed in California in 1926. Doctor Verbryck was a member of the Los Angeles County Medical Association.

# PUBLIC HEALTH REPORT

**LESTER R. BRESLOW, M.D.**  
**Director of Public Health**

AT THE SEMI-ANNUAL meeting of the Cancer Advisory Council held in Los Angeles on 13 April 1966, David A. Wood, M.D., director of Cancer Research Institute and professor of pathology at the University of California Medical Center in San Francisco, was unanimously elected chairman for the coming year, replacing Joseph F. Ross, M.D., professor of medicine at the University of California School of Medicine in Los Angeles. At the same meeting, Jesse L. Steinfeld, M.D., associate professor of medicine at the University of Southern California School of Medicine, was elected vice chairman, succeeding Dr. Wood.

The Cancer Advisory Council is a 15-member group authorized by a law passed by the 1959 State Legislature to assist the State Department of Public Health in the enforcement of the same law which was designed to curb medical quackery in cancer diagnosis and treatment in the State of California. The Council is composed of physicians, other scientists and lay persons appointed for staggered four-year terms by the Governor and the Director of Public Health, who is an ex-officio member. The current membership is as follows:

David A. Wood, M.D., chairman, San Francisco  
Jesse L. Steinfeld, M.D., vice chairman, Los Angeles  
Lester Breslow, M.D., Director of Public Health and ex-officio member, Berkeley  
Sol R. Baker, M.D., Beverly Hills  
Mrs. Robert L. Brown, Reseda  
John W. Cline, M.D., San Francisco  
Mr. Emanuel Fineman, Los Angeles  
L. H. Garland, M.D., San Francisco  
Edith R. Lindly, Ed.D., Fresno  
Thomas S. Nelsen, M.D., Palo Alto  
O. B. Pratt, M.D., Los Angeles  
Joseph F. Ross, M.D., Los Angeles  
Sol Silverman, Jr., D.D.S., San Francisco  
M. H. Simmers, M.D., Los Angeles

There is one vacancy.

During its existence, the Cancer Advisory Council has found eight cancer diagnosis or treatment

agents valueless and has recommended that regulations prohibiting the prescription, administration, sale or other distribution be adopted by the State Board of Health on seven of these. Action is pending on the eighth. Five of the seven against which regulations have been adopted have been used in the "treatment" of cancer—the Hoxsey remedy, Koch antitoxin, Laetrile, Lincoln staphage lysate, and Mucorhycin. The two others, the Anthrone and Bolen tests, have been used in the "diagnosis" of cancer.

During the same period, cease and desist orders have been issued against 15 practitioners.

These orders were concerned with the banned agents listed above as well as 14 others whose use by certain cited individuals was prohibited under a feature of the law which does not require a prohibitory regulation. Court appearances are scheduled for two others, a lay person in the San Diego area and a Fresno chiropractor.

An investigatory unit of the Department of Public Health performs preliminary investigation following complaints by physicians, surviving relatives, welfare organizations, better business bureaus, American Cancer Society branches, county medical societies and others, assembles evidence pertaining to the investigation and arranges for such testing as might be indicated and recommended by the Council. Following consideration of the evidence, the Council may recommend that action leading to a prohibitory regulation or a cease and desist order be undertaken by the Department of Public Health. The Department may or may not take action upon this recommendation. In the first instance, if the Department does act upon the recommendation of the Council, a proposed regulation is submitted to the State Board of Public Health, which is the unit authorized to perform such action. In all instances, the Council and the Department are counseled by members of the Attorney General's office who also present the



cases in instances where action goes before a hearing officer.

Support of all practicing physicians and of all governmental or private agencies in the State is needed in order to further the program and is earnestly solicited. This support may take any or all of the following forms:

1. When treatment of patients with unproven methods comes to the attention of any physician, society, bureau or other agency, the local county medical society, the local health officer or the local branch of the American Cancer Society should be notified and requested to pass the information on to the State Department of Public Health, 2151 Berkeley Way, Berkeley 4, California. The latter agency may also be notified directly by mail or telephone to Dr. K. F. Ernst, 843-7900, extension 321.

2. When a questionable situation comes to the attention of a physician, historical notes to record methods of diagnosis, claims for and details of treatment, name of the treatment and of the clinic or individual offering it, and the cost of the treatment, should be made while still fresh in the patient's mind. If it is suspected that the diagnosis of cancer is false, diagnostic studies which may confirm the diagnosis or show that it is incorrect should be performed after making arrangements with the State Department of Public Health. Objective findings for comparison with those before treatment, if known by the physician or stated by the patient, should be recorded.

Factual or opinion testimony by physicians or other scientists regarding physical findings or the efficacy of a given remedy is of great value when court or administrative action is being considered.



# INFORMATION

## Tape Recordings in Medical Education

### *The Pioneering Role Played by the California Medical Association's Audio-Digest Foundation*

CLARON L. OAKLEY, B.S.J., M.S.J., Los Angeles

LAST YEAR, to commemorate the Audio-Digest Foundation's twelfth anniversary of California Medical Association's sponsorship, we wrote personal letters of thanks to those subscribers who (624 hours of listening later) had been with us from our first year. We acknowledged their personal contribution to our success, then asked them how our tape-recorded subscription service had been useful in their own practice. There have been hundreds of replies, many of them typed or handwritten by the physician himself, and some that go on for as many as four pages.

Revealing the diverse ways in which the tapes are utilized, here are some representative abstracts:

"Three GP's share our one subscription. I listen in the bathroom while getting ready for work, as well as in the automobile, while on house calls."

"As I am a ham operator, I listen to the tapes in my ham shack, where I'm alone and things are quiet."

"It seems to me that the authoritative voices heard on the tape leave a more lasting impression than reading an article or looking at charts. I have two recorders set up for listening: one by my bed for 15 minutes' listening each night; another in my car to listen while traveling between home, hospital and office. I also use the car recorder to dictate reports and charges on my house calls while they are still fresh in my mind."

"By a flip of a switch, I listen and learn from the leaders of medicine all over America, at a minimum expenditure of cost and time. Many times, I've learned about a new drug, from an unbiased viewpoint, long before the detail man tries to 'sell' me on it. My recorder is in my desk drawer at the office, so I can listen to the tape in brief snatches during a lunch hour or between-patients break."

"I use your tapes as an adjunct to a residency teaching program at Fitzsimmons Army Hospital. The topics serve as a basis for discussion groups, with residents, interns, and medical students participating."

"I enjoy listening to the tapes in the quiet atmosphere of our hospital medical library reading room, where they

are always available and where the information heard can be correlated with other reading material if necessary."

"Over these 10 years, I've enjoyed listening to Audio-Digest while sitting in an easy chair, while making calls in my automobile, and even while cooking."

"I've taken the tapes to Journal Clubs, house staff meetings, and to augment teaching rounds at various hospitals where I have attending duties. On occasions I supply my colleagues with some of the tape information as background material for their lectures."

"You won't believe it—but I listen to many of my tapes while flying my Cessna around the Jackson Hole country, making my rounds of isolated hospitals and clinics. I have to strain to hear over the airplane motor, but it's worth it!"

Remembering our provincialism of just a few years ago, it is fascinating now to scan the origins of hundreds of new orders—and renewals—that arrive in the circulation offices: A U.S. Navy installation in Yokosuka, Japan (whose tapes are used in a journal club with local Japanese physicians, who remark that Audio-Digest not only updates their medical knowledge, but also improves their English); Air Force bases in such remote areas as McMurdo Sound in the Antarctica, Thule Air Force Base in Greenland, and seven stations in Europe and the Mediterranean; an American oil company in Saudi Arabia; the Indian Medical Association in Hyderabad, India; the South African Medical Association in Johannesburg.

The U.S. Department of State distributes the tapes via diplomatic pouch to its foreign embassies. Recently, the Bolivian Embassy asked permission to duplicate a program on amebiasis to distribute among 15 medical stations in that country.

Private subscriptions arrive daily from such far-flung spots as Nazareth, Manila, Singapore, Seoul, Taipei, Sydney, Dublin and Paris. Although it does not appear on our subscription roster, the Pavlov Institute in Russia is known to receive the tapes regularly via some anonymous benefactor.

Hundreds of tapes are donated by subscribers to the Christian Medical Society each month and are circulated, round robin, to the darkest corners of Africa, South America and other isolated parts of the earth. Before his murder in the Congo, Dr. Paul Carlson was a regular listener to the tapes.

The volunteer staff of "Project Concern," a non-profit private enterprise engaged in donating medical care to refugees, listens to the tapes on a floating hospital ship in Hong Kong's Aberdeen Harbor every Saturday morning, then sends them on to the Project's newly-opened installation in South Viet Nam the following day.

The author is vice president and editor, Audio-Digest Foundation.



American physicians volunteering for short-term medical duty in South Viet Nam are being kept abreast of medical developments through donated Audio-Digest subscriptions set up through MIL-HAP (Military Provincial Hospital Assistance Program).

Gratuitous subscriptions have also just been allocated to the World Federation of Societies of Anesthesiologists. With the goal of helping this organization upgrade anesthesia care and teaching in three widely-separated parts of the globe, Audio-Digest will be contributing continuing subscriptions to centers in Latin America, Asia and Africa.

In Australia, the tapes are incorporated into a telephonic cross-country educational system piped into key hospitals in all parts of the continent. Arrangements are also underway to exchange taped clinical material with Britain's College of General Practitioners and the British Ophthalmic Tape Reports.

It is little wonder that members of our editorial staff feel they are engaged in an important and humanitarian endeavor when they read letters like these:

From the U.S. Secretary of State's Clinical Director: "The Audio-Digest tapes meet an ideal need of our medical division. Our physicians on long tours of duty in the developing countries feel they are still in contact through your excellent communication medium."

From the African Medical and Research Foundation in Kenya: "This is to express appreciation for the Audio-Digest tapes. We have a radio network linking 50 bush mission hospitals to a central clearing station. Your tapes enable us to upgrade that advisory service to what is, in effect, a postgraduate teaching program by radio. This is a most significant contribution to medical progress in these young nations."

From the Baptist Hospital in Nigeria: "I could never say how much pleasure it is to hear some authoritative medical discussions when one is the only doctor for miles in all directions."

From the Seventh-Day Adventist Hospital in Bandung, Indonesia: "May I say that we have found your tapes very valuable in keeping abreast with the medical world with a minimum of time and effort—and especially so in this area of the world where facilities for postgraduate work are so sparse."

From Headquarters, 8th Infantry Division, U.S. Army: "Here in Germany, we find your tapes to be an excellent medium for stimulating our physicians in their professional thinking. Often, the younger physician finds himself burdened with administrative or training functions so that he feels himself to be retrogressing professionally. Your tapes provide a means to combat these impressions."

Here in America, the majority of leading teaching centers subscribe to one or more of the seven different services, and some subscribe to all of

them. The Central Intelligence Agency (for reasons known only to itself) subscribes to the General Practice and Internal Medicine services, as does the National Institutes of Health.

Even while growing rapidly, Audio-Digest staff strives to maintain a close inter-family relationship with its world-wide roster of subscribers. Every letter received is promptly and personally answered; and, through questionnaires at frequent intervals, close touch is kept with the physician-listener's ideas and opinions. This, plus the listener's apparent satisfaction with the tape-recorded method of keeping abreast of medical advances, has enabled us to reach an overall subscription renewal rate of more than 75 per cent. Some services (Ophthalmology and Anesthesiology, for example) approach an average of 85 per cent. And among subscribers who have remained with us for at least three years, the renewal rate from then on climbs to an amazing 90 per cent. This (despite the costly subscription pricetag of \$81.50 a year) exceeds the renewal averages of such national magazine institutions as *Time*, *Life* and *Reader's Digest*.

What advantages in this method have led to its phenomenal acceptance among the medical profession? Among the most important, we believe, are these:

- We have shown that for some physicians the spoken word has a power to command and hold attention that the printed word has not. It takes far more than italics and boldface type to convey a lecturer's intended expression, timing and emphasis. Indeed, many subscribers—after hearing a lecture filled with the enthusiasm and fire of a Philip Thorek, Paul Dudley White, or Sydney Gellis, to name just a few—remark that they feel they have had a personal conference with the expert.

- This carefully pre-selected medical programming insures the physician against self-selected education and substitutes what other expert teachers feel is important, thus broadening his experience.

- The relatively expensive subscription makes it incumbent upon the physician to get his money's worth by listening from beginning to end. There is no easy way to jump from place to place in the tapes; therefore, the programs are heard in their entirety.

- The tapes make use of otherwise wasted segments of time for the busy physician. He can listen while driving his car, or dressing, shaving or eat-

ing. Some play the tapes while pursuing a hobby such as woodworking or painting.

- The tapes erase geographical isolation for many physicians. Through our ability to record and reproduce in quantity the voices of the best teachers, the faculties of Harvard, Mayo Clinic, Lahey Clinic, and all the great teaching centers can be brought to the doorstep of the most remotely located physician.

- This medium is able to capture for the listeners the sound and nuances that black print never can: the voice quality of a Parkinsonian patient as his history is related to a resident in neurology; the heart sounds of various forms of cardiac disorders; peristaltic bowel sounds in different kinds of intestinal obstruction; and many other situations where the voice or body can speak more loudly than the printed word.

- The tapes make an excellent springboard for journal club or staff discussions. They can make a hospital luncheon hour a fruitful exchange of information; or they can be incorporated into inter-resident teaching programs as supplementary methods of instruction.

- One of the great historic values of the medium is its ability to retain for posterity the voices of some of the contemporary great men in the world of medicine. In our archives, for example, are recorded reminiscences of the discovery of penicillin by Sir Alexander Fleming, as well as numerous lectures and informal discussions by such late and great physicians as Sara Jordan, Richard Cattell, Champ Lyons and (names well-known to Californians) Lowell Rantz, Francis Hodges and Charles D. Armstrong.

One of the California Medical Association's original motivations in accepting ownership of Audio-Digest from Mr. Jerry L. Pettis was the prospect that its operation might not only make an educational contribution to American medicine, but a continuing financial one, as well. That this prospect has been realized is demonstrated in the fact that, over the past 12 years, more than \$300,000 has been contributed from excess reserves to the American Medical Association's Education and Research Foundation and to the California Medical Education and Research Foundation.

Booked orders stand at well over \$700,000 for the current fiscal year; and the amount is expected to reach \$1 million during 1967.

A portion of the CMERF contribution has been used to finance freshman scholarships to the new University of California, California College of Medicine, Los Angeles. Each of the recipients has taken time to write the Board of Trustees to express appreciation for the bequest; and the spirit of the letters is neatly digested by a phrase in one received earlier this year: "Thank you so much for alleviating one freshman's worries about the cost of his medical education. It is my wish and my duty to make good on the faith you have demonstrated, by doing all I can to become an outstanding physician of the future."

Both in and out of the medical profession, there have sprung up from time to time sincere imitators of our audio medium and format. None, however, has been able to meet with any enduring success, since the majority have depended upon fickle pharmaceutical-house financial support, have been motivated solely by considerations of profit, and have lacked the medical profession's overall approbation and cooperation.

From an editorial standpoint, we feel that our succeeding—where others subsequently fail—is due, in large part, to the Foundation's actually being part and parcel of organized medicine by virtue of its CMA ownership. Because of this, the American Medical Association and the American College of Obstetricians and Gynecologists were among the first national organizations to open their doors to on-the-spot recordings of their annual meetings by Audio-Digest. Stimulated by their example, other distinguished national specialty organizations, as well as leading medical schools and teaching centers, have also consented to disseminate highlights of their scientific meetings and refresher courses through the subscription facilities of Audio-Digest.

Prominent among these cooperating groups that have immeasurably helped to make this operation a success are the American College of Physicians, the American Society of Anesthesiologists, American Academy of Ophthalmology and Otolaryngology, International College of Surgeons, Pan-Pacific Surgical Association, and more than 150 others.

Within the obvious limitations of teaching by ear alone, Audio-Digest has successively and successfully launched seven different specialty publications since its inception—beginning with a weekly General Practice series and adding, over the years, Internal Medicine, Obstetrics and Gynecology, Surgery, Pediatrics, Anesthesiology and Ophthalmology.



When another 10 years have gone by, we are confident that swiftly advancing electronic techniques will enable us not only to join the eye with the ear in the specialties we already serve, but also to add many other specialized areas to our present coverage. Primarily, this is envisioned through the innovation of videotape recorders that will allow us to tape-record not only speakers' voices, gestures, and facial expressions, but also their visual presentation of slides, charts, and photographs of illustrative case histories. Home video recorders and playback units are still in a prohibitive price

range for mass production and distribution; but indications are that it is only a matter of time before they can be obtained for the same price that is now paid for a good audio-only tape recorder.

When that day comes, the Audio-Digest Foundation, in continuing the objectives laid down by its founders, intends to be prepared to chart still other significant areas in this complicated and crucially-important problem of *continuing* postgraduate medical education for the practicing physician.

Audio-Digest Foundation, 619 South Westlake Avenue, Los Angeles, California 90057.



# NEWS & NOTES

NATIONAL • STATE • COUNTY

## LOS ANGELES

**Dr. Roy F. Perkins**, Alhambra, has been named director of the American Medical Association's newly established Department of Health Care Services.

The department will be concerned with community health services, voluntary health agencies, aging, maternal and child care, group practice, insurance and prepayment, patterns for the organization and delivery of medical care, manpower, and the business side of medical practice.

\* \* \*

**Dr. John W. Dorsey**, Long Beach, was installed as president of the western section of the American Urological Association at a recent meeting of the organization. Dr. Dorsey had served the section as secretary-treasurer for six years.

\* \* \*

The forty-third annual conference of the **American Physical Therapy Association** is scheduled for 10 to 15 July 1966, at the Biltmore Hotel in Los Angeles, California.

## SAN FRANCISCO

**Dr. Dwight L. Wilbur**, clinical professor of medicine, Stanford University School of Medicine, and editor of **CALIFORNIA MEDICINE**, was awarded the **Julius Friedenwald Medal** of the American Gastroenterological Association for 1966. Given for "outstanding achievement in gastroenterology," the medal was presented at the association's annual meeting in Chicago, 27 May.

\* \* \*

A clinic for children with specific learning disorders is being established at the University of California San

Francisco Medical Center. Physicians who specialize in disorders of the nervous system, psychologists, specialists in speech and hearing problems, social workers, and specially trained teachers will work with pediatricians to evaluate and treat the children and counsel the parents.

The new clinic, in addition to providing a service for patients, will be a **training source for future physicians** specializing in child care and a demonstration clinic for community service personnel who work with children, including teachers, school psychologists and juvenile court personnel.

## SANTA CLARA

**Dr. Emmet J. Lamb**, assistant professor of gynecology and obstetrics at Stanford University School of Medicine, has been awarded one of 10 **Macy Faculty Fellowships in Obstetrics** by the Josiah Macy Jr. Foundation of New York.

The 10 grants total \$450,000 for three years and are designed to meet basic salaries of young staff members and encourage their commitment to academic obstetrics. The recipients were chosen from candidates submitted by 37 medical schools.

## GENERAL

Applications have been invited for National Institutes of Mental Health **fellowships in child psychiatry** to begin 1 July 1967. The fellowships are open to pediatricians, general practitioners, or physicians who are at least five years out of medical school, are United States citizens, and have had approved medical and internship training. The stipend is \$10,000 a year. The Fellowship provides an intensive orientation in all areas of child and adolescent psychiatry.

Further information may be obtained from **Dr. Joseph D. Teicher**, Los Angeles County General Hospital, 1934 Hospital Place, Los Angeles.

\* \* \*

The 12th annual meeting of the **Flying Physicians Association** will be held at the Dunes Hotel, Las Vegas, 11 to 16 September, according to **Dr. Marvin B. Hays**, Eureka, who heads the association's California chapter of 213 members.





# EDUCATION NOTICES

## Meetings and Courses

### COMMITTEE ON CONTINUING MEDICAL EDUCATION

THIS BULLETIN of the dates of continuing education programs and the meetings of various medical organizations in California is supplied by the Committee on Continuing Medical Education of the California Medical Association. In order that they may be listed here, please send communications relating to your future meetings or postgraduate courses to Committee on Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco, California 94102.

#### KEY TO ABBREVIATIONS AND SYMBOLS

Medical Centers and CMA Contacts  
for Postgraduate Course Information

CMA:	California Medical Association For information contact: Continuing Medical Education, California Medical Association, 693 Sutter Street, San Francisco 94102. PROspect 6-9400, Ext. 68.
LLU:	Loma Linda University For information contact: W. F. Norwood, Ph.D., Associate Dean, Continuing Education, Loma Linda University School of Medicine, 1720 Brooklyn Ave., Los Angeles 90033, ANgeles 9-7241, Ext. 214.
PRES.	Presbyterian Medical Center
MED. CTR.	For information contact: Arthur Selzer, M.D., chairman, Education Committee, Presbyterian Medical Center, Clay and Webster Streets, San Francisco 94115. WEst 1-8000.
UCLA:	University of California at Los Angeles For information contact: Donald Brayton, M.D., Assistant Dean for Postgraduate Medical Education, 15-39 Rehabilitation Center, University of California Center for Health Sciences, Los Angeles 90024, 478-9711, Ext. 4345.
UCSF:	University of California, San Francisco For information contact: Seymour M. Farber, M.D., Dean, Educational Services and Director, Continuing Education, University of California Medical Center, Room 565-U, San Francisco 94122, 666-1692.
USC:	University of Southern California For information contact: Phil R. Manning, M.D., Associate Dean, Postgraduate Division, USC School of Medicine, 2025 Zonal Ave., Los Angeles 90033, CApital 5-1511, Ext. 300.
STAN:	Stanford University For information contact: Roy Cohn, M.D., Associate Dean for Graduate Affairs, Stanford University School of Medicine, 300 Pasteur Drive, Palo Alto, DAVenport 1-1200.

### JUNE

June 17—Attending Staff Association of Olive View Hospital Symposium on Infectious Diseases. OVH, Olive View. Friday. Contact: Joseph K. Indenbaum, M.D., secretary-treasurer, ASAOVH, Olive View.

June 18-19—Medical Care of the Future—The Effects of Social Forces and Legislative Activities on the Patterns of Education, Health Facilities and the Provisions for Health Care. Medical Sciences Auditorium, UCSF. Saturday-Sunday. Proceedings will be telecast live over KQED and KVIE. Arrangements have been made to provide direct two-way communication with various Northern California hospitals. Contact UCSF for further information.

June 22-24—Highlights of Modern Ophthalmology. Lions Eye Bank. Wednesday-Friday. 8 hours daily. \$75. Contact: Eva del Oro, secretary, Lions Eye Bank, 2018 Webster Street, San Francisco.

June 22-24—Treatment of Fractures. USC. Wednesday-Friday.

June 23-25—SACRAMENTO VALLEY COUNTIES—Regional Postgraduate Institute presented by California Medical Association in cooperation with Stanford. Harvey's Resort Hotel, Lake Tahoe. Thursday noon-Saturday noon. \$15. "Advances in Therapy: Diseases of Medical Progress, Newer Antibiotics, Peptic Ulcer Disease, Cosmetic Plastic Surgery." Chairman: John N. Miller, Jr., M.D., 5301 F Street, Sacramento.

June 25—Diagnosis and Management of Infectious Diseases. Amphitheater Conference Room, Children's Hospital of Orange County, 1109 W. La Veta, Orange 92666. Saturday, 8:30 a.m. to 4:00 p.m. \$5 (lunch included). Contact: Merl J. Carson, M.D., Medical Director, CHOC.

June 29-July 1—Pediatric Seminar. Children's Hospital, 8001 Frost Street, San Diego 92133. Wednesday-Friday. \$25. Contact: Thelma Brown, Community Relations, Children's Hospital.

### JULY

July 2-6—Seminars for General Practitioners. UCLA at Lake Arrowhead. Saturday-Wednesday. 18 hours. \$110.

July 10-12—Hospital Infections Control. Neuropsychiatric Institute Auditorium, 720 Westwood Plaza Bldg., No. C-18-183, West Los Angeles. Sunday-Tuesday. Contact: John W. Brown, M.D., Bureau of Communicable Diseases, Department of Public Health, 2151 Berkeley Way, Berkeley 94704.

July 30-August 10—Annual Postgraduate Refresher Course in Honolulu and Kauai. USC. Saturday-Wednesday. 43½ hours. \$125.

### AUGUST

August 7-10—Advanced Seminars in Pediatrics. "Immunologic Principles and Their Clinical Applications." UCLA at Lake Arrowhead. Sunday-Wednesday. 15 hours. \$110.

August 12-13—National Conference on Infant Mortality. Fairmont Hotel, San Francisco. Friday-Saturday. Contact: Harold S. Morgan, M.D., chairman, Committee on Maternal and Child Care, American Medical Association, 535 North Dearborn Street, Chicago, Illinois 60610.

August 13-14—**Obstetrics and Gynecology.** UCLA. Saturday-Sunday. 16 hours.

August 17-21—**Advanced Seminars in Dermatology.** UCLA at Lake Arrowhead. Wednesday-Sunday. 15 hours.

August 21-24—**Advanced Seminars in Internal Medicine.** UCLA at Lake Arrowhead. Sunday-Wednesday. 15 hours. \$110.

August 27—**American Institute of Ultrasonics in Medicine.** Sheraton Palace Hotel, San Francisco. Saturday. Contact: John H. Aldes, M.D., executive director, 4833 Fountain Avenue, Los Angeles 90029.

August 28—**American Association of Electromyography and Electrodiagnosis.** Sheraton-Palace Hotel, San Francisco. Sunday. Contact: Max Karl Newman, M.D., director, 16861 Wyoming Avenue, Detroit 48221.

August 28-31—**Medicine and Religion.** UCLA at Lake Arrowhead. Sunday-Wednesday. 15 hours.

August 28-September 2—**American Academy of Physical Medicine and Rehabilitation.** Sheraton-Palace Hotel, San Francisco. Sunday-Friday. Contact: Harriet E. Gillette, M.D., secretary, Cleveland Clinic, Cleveland.

## SEPTEMBER

September 8-10—**Saint John's Hospital Annual Postgraduate Assembly.** SJH, 1328 22nd Street, Santa Monica. Thursday-Saturday. Contact: John C. Eagan, M.D., director, SJH.

September 10-11—**Health of the School Child.** UCSF. Saturday-Sunday.

September 13-November 29—**Emergency Management of the Acutely Ill Patient.** USC at Los Angeles County Hospital. Tuesday evenings. 18 hours. \$80.

September 14-16—**Hospital Infections Control.** Auditorium, Medical Sciences Bldg., UCSF. Wednesday-Friday. Contact: John W. Brown, M.D., Bureau of Communicable Diseases, Department of Public Health, 2151 Berkeley Way, Berkeley 94704.

September 14-December 21—**Psychotherapeutic Principles and Practice for Non-Psychiatrists.** UCSF. Wednesdays.

September 15-16—**Current Concepts in Obstetrics and Gynecology.** USC. Thursday-Friday. 14 hours.

September 15-16—**Merritt Hospital Medical Seminar.** Claremont Hotel, Berkeley. Thursday-Friday. 10 hours. Contact: Robert R. Crosbie, M.D., secretary of the Staff, MH, Hawthorne and Webster, Oakland.

September 16-17—**Advances in Electrocardiography.** Sponsored by Daniel Freeman Hospital, 333 N. Prairie Ave., Inglewood. To be held at the Statler Hotel and Los Angeles County Medical Association Bldg., Los Angeles. Friday-Saturday. 10 hours. \$15 members, \$25 non-members. Contact: W. Graf, M.D., chairman, 3701 Stocker Street, Los Angeles 90008.

September 16-18—**New Concepts in the Management of Common Ailments of the Human Foot.** UCSF. Friday-Sunday.

September 17—**Annual Symposium on Cardiovascular Disease.** Sponsored by the Heart Associations of Ventura and Santa Barbara Counties. Biltmore Hotel, Santa Barbara. Saturday. 6 hours. \$12.50. Contact: Sara Clyde, executive director, 18 La Arcada Court, Santa Barbara.

September 17-18—**Group Psychotherapy.** UCSF at Mendocino State Hospital, Talmage. Saturday-Sunday.

September 19-May 22—**Radiological Physics.** UCSF. Monday evenings.

September 20-October 25—**Specific Syndromes Associated with Mental Retardation.** UCSF at Sonoma State Hospital, Eldridge. Tuesdays.

September 20-December 6—**Medical Radio Conferences.** UCSF. Tuesdays.

September 21-23—**Recent Advances in Internal Medicine.** UCSF. Wednesday-Friday.

September 21-24—**Surgical Pathology of the Eye.** UCSF. Wednesday-Saturday.

September 22-December 15—**Bedside Clinics and Set Clinics in Internal Medicine.** USC. Thursday evenings. 24 hours. \$80.

September 23—**Annual Symposium of the Northern California Chapter, National Kidney Foundation.** UCSF. Friday.

September 24-25—**Progress in Psychiatry.** UCSF at Sutter Memorial Hospital, Sacramento. Saturday-Sunday.

September 24-25—**Child Psychiatry.** UCSF at Napa State Hospital, Imola. Saturday-Sunday.

September 26—**Society for Pediatric Radiology.** Hilton Hotel, San Francisco. Monday. Contact: John L. Gwinn, M.D., treasurer, Children's Hospital, 4614 Sunset Blvd., Los Angeles 90027.

September 26-October 7—**Intensive Review of Internal Medicine.** USC. Mornings daily for 2 weeks. 40 hours. \$80.

September 27-30—**American Roentgen Ray Society.** Hilton Hotel, San Francisco. Tuesday-Friday. Contact: C. Allen Good, M.D., executive secretary, Mayo Clinic, 200 First Street, SW, Rochester, Minn. 55901.

September 28-29—**Los Angeles County Heart Association Annual Symposium on Heart Disease.** Statler Hilton Hotel, Los Angeles. Wednesday-Thursday. 12 hours. Contact: Professional Symposium Committee, 2405 West Eighth Street, Los Angeles 90057.

September 28-30—**Annual Postgraduate Symposium on Heart Disease.** Sponsored by San Francisco Heart Association. St. Francis Hotel, San Francisco. Wednesday-Friday. 18 hours. \$35. Contact: Gene C. Taylor, executive director, SFHA, 259 Geary Street, San Francisco.

September 28-30—**American Association of Medical Clinics.** Hotel Del Coronado, San Diego. Wednesday-Friday. Contact: Edwin P. Jordan, M.D., executive director, P.O. Box 58, Charlottesville, Va. 22902.

September 30-October 1—**Annual Professional Symposium on Heart Disease.** Town and Country Hotel, San Diego. Friday-Saturday. 12 hours. \$5. Contact: James E. Lasry, M.D., chairman, San Diego County Heart Association, 3545 Fourth Avenue, San Diego 92103.

## OCTOBER

October 1—**Shufelt Society of Santa Clara County Fall Seminar.** Obstetrics and Gynecology. Auditorium, Santa Clara County Administration Bldg., 70 West Hedding Street, San Jose. \$15. Contact: H. W. Christopher, M.D., secretary, 621 E. Campbell Avenue, Campbell.



October 4-November 15—**Isotope Techniques in the Health Sciences**. UCSF. Tuesdays.

October 5-November 30—**Evening Lectures in Medicine**. UCSF at Oakland Hospital, Oakland. Wednesdays.

October 6-8—**Newer Aspects of Obstetrics and Gynecology**. UCSF. Thursday-Saturday.

October 6-8—**American Association for Surgery of Trauma**. Santa Barbara Biltmore Hotel, Santa Barbara. Thursday-Saturday. Contact: Sawnie R. Gaston, M.D., secretary, 180 Ft. Washington Avenue, New York 10032.

October 7-December 16—**Medical Television Conferences**. UCSF. Fridays.

October 8-9—**Recent Developments in Nuclear Medicine**. UCLA. Saturday-Sunday. 16 hours.

October 8-9—**Stroke**. UCSF at St. Mary's Hospital, San Francisco. Saturday-Sunday.

October 10-14—**American College of Surgeons**. Fairmont Hotel, San Francisco. Monday-Friday. Contact: John P. North, M.D., director, 55 Erie Street, Chicago 60611.

October 10-14—**Pediatric Allergy**. UCSF. Monday-Friday.

October 11—**Northeastern California Chapter of the Arthritis Foundation Symposium**. Mercy Hospital, Sacramento. Tuesday. Contact: Harold B. Strauch, M.D., 4101 J Street, Sacramento 95819.

October 14-15—**Western Industrial Medical Association**. International Hotel, Los Angeles. Friday-Saturday. Contact: Ellsworth F. Marriner, M.D., secretary, Autonetics Division, North American Aviation, Inc., 3370 Miraloma Road, Anaheim 92803.

October 15-16—**Alcoholism**. UCSF. Saturday-Sunday.

October 16-20—**American Orthotics and Prosthetics Association**. Riviera Hotel, Palm Springs. Sunday-Thursday. Contact: Lester A. Smith, executive secretary, 919 18th St., NW, Suite 130, Washington, D.C.

October 18-November 22—**Neuropsychiatry in Daily Practice**. UCSF at Agnews State Hospital, San Jose. Tuesdays.

October 19—**Newborn Infant Care**. USC. Wednesday. 8 hours.

October 21-22—**Calcium**. UCSF. Friday-Saturday.

October 21-25—**Association of American Medical Colleges**. San Francisco Hilton Hotel, San Francisco. Friday-Tuesday. Contact: Robert C. Berson, M.D., executive director, 1501 New Hampshire Avenue, NW, Washington, D.C. 20036.

October 22-23—**Family Therapy**. UCSF at Modesto State Hospital, Modesto. Saturday-Sunday.

October 24-28—**Spinal Cord Injuries**. UCSF at Kaiser Foundation Rehabilitation Center, Vallejo. Monday-Friday.

October 27-November 1—**Pacific Dermatologic Association**. El Mirador Hotel, Palm Springs. Thursday-Tuesday. Contact: Mortimer S. Falk, M.D., secretary-treasurer, 503 S. Arlington, Reno, Nevada.

October 27-November 3—**American School Health Association**. Jack Tar Hotel, San Francisco. Thursday-

Thursday. Contact: A. O. DeWeese, M.D., executive secretary, 515 E. Main Street, Kent, Ohio 44240.

October 28—**Kern County General Hospital Postgraduate Conference (and Alumni Day)**. KCGH, 1830 Flower Street, Bakersfield. Friday. 8 hours. Contact: George A. Paulsen, M.D., KCGH.

October 29-30—**Practical Management of Surgical Problems**. UCSF at Franklin Hospital, San Francisco. Saturday-Sunday.

October 30-November 2—**California Academy of General Practice Annual Scientific Assembly**. El Cortez Convention Center, San Diego. Sunday-Wednesday. 13 hours. \$10.: non-members. Contact: William W. Rogers, executive secretary, CAGP, 9 First Street, San Francisco.

October 31-November 4—**American Public Health Association**. Civic Auditorium, San Francisco. Monday-Friday. Contact: Berwyn F. Mattison, M.D., executive director, 1790 Broadway, New York 10019.

October 31-November 4—**American Association of Public Health Physicians**. San Francisco. Monday-Friday. Contact: John S. Neill, M.D., secretary, P.O. Box 1731, Tampa, Florida 33601.

## NOVEMBER

November 2-3—**American College of Preventive Medicine**. San Francisco Hilton, San Francisco. Wednesday-Thursday. Contact: Robert E. Coker, Jr., M.D., executive secretary, P.O. Box 1263, Chapel Hill, North Carolina 27514.

November 4-6—**Executive Health**. UCSF. Friday-Sunday.

November 5-6—**Somatic Mask of Psychiatric Illness**. UCSF at Fresno Community Hospital, Fresno. Saturday-Sunday.

November 5-6—**Gastrointestinal Diseases**. UCSF at Children's Hospital and Adult Medical Center, San Francisco. Saturday-Sunday.

November 9—**Annual Science Lecture of the Southern California Region, American College of Physicians**. "Current Problems of Oceanography." Wednesday. 7:30 p.m. \$10. Contact: W. Philip Corr, M.D., governor, SCACP, 3660 Arlington Avenue, Riverside 92506.

November 9-10—**Workshop in Cardiac Arrhythmias**. USC. Wednesday-Thursday. 16 hours.

November 11—**Medicine in Surgery Symposium**. Sponsored by Fresno-Madera-Kings Counties Medical Societies. Del Webb Center, Fresno. Friday. 6 hours. Contact: Cam Covington, M.D., 2057 High Street, Selma.

November 12-13—**Annual Clinical Cancer Conference**. UCSF. Saturday-Sunday.

November 18-19—**Annual Staff Seminar: "Cancer of the Abdomen"**. California Hospital, 1414 South Hope Street, Los Angeles. Friday-Saturday. 10½ hours. \$15. Contact: K. L. Senter, M.D., CH.

November 18-19—**Orthopedics**. UCSF. Friday-Saturday.

November 28—**Medical Aspects of Well Being—Rehabilitation**. UCSF. Monday.

November 30-December 3—**Viral Diseases of the Eye**. UCSF. Wednesday-Saturday.

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### Transfusions for Unborn Infants

Two new methods for giving blood transfusions to a human fetus are reported in the May 16 *Journal of the American Medical Association*.

Both procedures are designed to help an infant survive when an immune reaction in the mother's body begins destroying the infant's red blood cells.

Ten years ago, about one in four such anemic infants died. Transfusions, though risky, have since 1963 cut the death rate to less than one in 10. A transfusion enables the infant to mature enough to survive a pre-term birth.

One method reported uses a television monitor and fluoroscopy, a constant-scanning x-ray, to ensure that the transfusing needle is accurately positioned after being passed through the mother's body and into the lower abdominal area of the fetus.

The second procedure uses a multiple-needle technique to transfuse fetuses as early as the 22nd week of gestation.

The fetus is an elusive target for a transfusion. It shifts position and responds to stimulation, such as the approach of a needle. Three investigators at Cornell University Medical College and the New York Hospital insert a first needle to literally pin down the infant. Usually placed in a fetal hip, this needle serves as a guide for inserting a second needle, which is used for the transfusion.

The technique minimizes the need for potentially harmful x-rays, its developers say. An average of only three x-ray exposures per transfusion was needed in the past 12 cases, the authors said. They are John T. Queenan, M.D., Gerald G. Anderson, M.D., and Philip B. Mead, M.D.

The other procedure also is designed to reduce radiation exposure and other hazards. About three minutes of direct television viewing as a single transfusion needle is inserted seems to them the safest approach, say three investigators at Boston University Hospital. Television monitoring eliminates the injection of "contrast fluid," sometimes used in x-ray procedure to define the area being studied.

By using television videotape, the Boston investigators are able to view the needle insertion a second time. This second look at needle position often reduces the need for further fluoroscopy, they said.

Authors of the report are Ernest J. Ferris, M.D., Jerome H. Shapiro, M.D., and Jacob Spira, Ph.D., all of the Boston University School of Medicine.

All of the investigators emphasized that intra-uterine transfusion remains a risky procedure. Even with greatest care, the transfusing needle can be misdirected and cause serious injury to the fetus.

"Nevertheless, because of the poor prognosis if the disease is left unattended, transuterine infusion

(Continued on Page 39)



## Medical Motion Pictures, Color TV to Be Daily Features at AMA Annual Convention

Medical motion pictures and color television will be a feature of the Annual Convention of the American Medical Association again this year.

The Convention is to be held in Chicago June 26 to 30, the Scientific Program at McCormick Place and the House of Delegates at the Palmer House.

Medical motion pictures have become an integral part of the Annual Convention program. Motion pictures are carefully screened and selected for quality, content and diversity of subject matter. Some are chosen from the AMA library of medical motion pictures while others are picked from among films just completed. Several new films are usually shown for the first time at the Annual Convention. The total motion picture program is thus planned to achieve both variety and currency.

Both medical motion pictures and color television will be presented daily. Live color television presentations have proven a popular addition to the Annual Convention Scientific Program. Like the movie program the color television program is carefully planned to put the unique educational potential of television at the service of continuing medical education. At last year's Convention in

New York, color television cameras took physicians into an operating room to watch surgical procedures.

Several of the Scientific Sections will participate in this year's color television program.

The Scientific Program for the 1966 Annual Convention was published in the May 9 issue of the *Journal of the American Medical Association*.

## Transfusions for Unborn Infants

(Continued from Page 38)

is gaining momentum," said the Boston investigators.

Close cooperation between obstetrician and radiologist can make it a safe procedure, they said.

Even as transfusion techniques improve, however, other medical research may be making them obsolete, says a *Journal* editorial in the same issue. New methods of preventing the red-cell destroying antibodies in maternal blood are under investigation.

First results have been good when large amounts of gamma globulin were administered to mothers to prevent the immune reaction.

"It is possible that in the near future the use of gamma globulin can markedly decrease the incidence of maternal immunization. In this way, some day, the intrauterine transfusion may become a discarded technique," the editorial said.



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## AMA Award to Dr. William B. Castle

The Joseph Goldberger Award in Clinical Nutrition will be presented this year to William Bosworth Castle, M.D., an American physician internationally known for his investigations of nutritional and hemolytic anemias.

The Goldberger Award of one thousand dollars and a plaque is presented annually by the Council on Foods and Nutrition of the American Medical Association and the Nutrition Foundation, Inc., to a physician who has made significant contributions to the knowledge of nutrition. Recipients are nominated by the Council and selected by the AMA Board of Trustees.

Dr. Castle will receive the award June 29 at the Scientific Awards Dinner to be held during the AMA Annual Convention in Chicago.

Dr. Castle graduated from the Harvard Medical School in 1921 and has been associated with the school and Boston hospitals ever since. He became a full Professor of Medicine at Harvard in 1937, George Richards Minot Professor of Medicine in 1957, and Francis Weld Peabody Faculty Professor of Medicine in 1963 upon his retirement from hospital administrative positions. Long associated with the Thorndike Memorial Laboratory of the Boston City Hospital, he served as its director from 1948 to 1963. At the Thorndike Laboratory, Dr. Castle worked under both Dr. Peabody and Dr. Minot, the men whose names were given to his last two chairs of medicine.

The Goldberger Award is being given to Dr. Castle "in recognition of significant clinical and laboratory contributions to the understanding of pernicious anemia and other blood diseases." His scientific publications number more than 150.

The pathologic physiology of nutritional and hemolytic anemias has been Dr. Castle's chief interest. He and his associates developed the concept of pernicious anemia as a deficiency of vitamin B12. They explained the deficiency as a manifestation of defective assimilation of the vitamin in the intestinal tract, often due to lack of necessary substance called intrinsic factor in the secretions of the stomach.

In another series of investigations, Dr. Castle and his associates explained the role of the spleen as a mechanical filter which screens misshapen or otherwise defective red cells from the blood.

In 1931-32, Dr. Castle was Director of the Rockefeller Foundation Commission for Study of Anemia in Puerto Rico. His studies showed that injections of crude liver extract saved the lives of persons suffering from sprue, and that treatment with iron rapidly cured anemia associated with hookworm disease even without removal of the parasites.

Fellowships in clinical nutrition offered by the AMA Council on Foods and Nutrition will carry Dr. Castle's name for the next academic year.





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**CLINICIAN**—Position available in Respiratory Disease Department for clinician interested in complete evaluation and management of pulmonary diseases. Salary starts at \$13,500 for Board eligible internist. Short-term appointments may be considered. Contact W. Y. Hallett, M.D., City of Hope Medical Center, 1500 East Duarte Road, Duarte, California 91010.

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#### KEY TO ABBREVIATIONS USED

(BRP)—Bureau of Research and Planning; (CMA)—California Medical Association; (CR)—Case Report; (CS)—Cancer Studies; (Ed.)—Editorial; (I)—Information; (LE)—Letter to Editor; (MSC)—Medical Staff Conference; (Or.)—Original Article; (PE)—Page End; (RSB)—Report of Scientific Board.

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